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INFECTIVITY OF THE PRIMARY COMPLEX OF TUBERCULOSIS OF CHILDHOOD

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Rich,[1] in his recently published critical review of the evidence for the existence of acquired resistance to tuberculosis in the human being, emphasized particularly two circumstances that provide strong support for the premise that acquired resistance not only is possible but actually exists. One concerns the generally accepted observation that the establishment and subsequent arrest of the primary complex are seldom followed by the occurrence and development of similar lesions even though opportunities for fresh extraneous infection are great. The second circumstance concerns the sequence of events that characterize the development and subsequent regression of the lesions of the primary complex in the great majority of instances. These lesions eventually cease to be progressive, become surrounded by connective tissue elements and if caseous eventually calcify. Rich, therefore, logically assumed that factors of resistance that were either absent or inadequate when the lesions were initiated are in most instances, as a consequence of the infection, sufficiently activated to bring the lesion of the primary complex under control. As a consequence, tubercle bacilli capable of further harm are eliminated from the lesions.

The evidence that lesions of the "primary complex" are arrested or "healed" and hence are unlikely to contain living tubercle bacilli is based on (1) studies of the morphologic changes as determined by histologic examination of the tissues and (2) studies in which material from the lesions of the primary complex was used to inoculate the highly susceptible guinea pig. The latter procedure is to be preferred if definite rather than presumptive evidence is desired.

According to Rich,[2] it has been shown by Zarfl, Blummenberg, Ghon and Potoschnig that the young Ghon tubercle contains many stainable, acid-fast bacillary forms. Rich[1] described a primary lesion in a 5 month old infant in which only a scant number of acid-fast bacilli could be found on staining. In older lesions in patients in the later decades, Schrader,[3] Feldman and Baggenstoss,[4] Anders[5] and others showed that in only a small percentage of the cases could viable tubercle bacilli be demonstrated in the primary complex by animal inoculation tests. It is well known that if the child is an infant at the time of infection the infection is more likely to spread beyond the limits of the primary parenchymatous lesion and the adjacent lymph nodes and lead to the death of the patient as a result of miliary tuberculosis, tuberculous meningitis or tuberculous caseous pneumonia.

It would appear important to determine how frequently viable tubercle bacilli can be shown by animal inoculation to be present in the primary complex of children dying from causes other than tuberculosis. Also of interest would be the histologic picture of the primary lesion as indicative of activity and the relationship of the character of the lesion to the presence of tubercle bacilli. Such a study should provide results indicative of the length of time that lesions of the primary infection in children retain their infectivity.

MATERIAL AND METHODS

During a period of six years, material representing 29 different cases was obtained. Except those that were obtained locally, the specimens were received by mail.[6] Approximately one half of the specimens were packed

From the Division of Experimental Medicine, Mayo Foundation, and the Section on Pediatrics, Mayo Clinic.

1. Rich, A. R.: The Pathogenesis of Tuberculosis, Springfield, Ill., Charles C Thomas, Publisher, 1944, pp. 460-493.

2. Rich,[1] p. 484.

3. Schrader, G., cited by Rich.[1]

4. Feldman, W. H., and Baggenstoss, A. H.: The Residual Infectivity of the Primary Complex of Tuberculosis, Am. J. Path. **14**:473 (July) 1938.

5. Anders, H. E., cited by Rich.[1]

6. Those who cooperated in this study by making available specimens for subsequent laboratory procedures were: Dr. Marian Barnes, Children's Memorial Hospital, Chicago; Dr. Martha E. Madsen, Children's Hospital, Detroit; Dr. Maud L. Menten, Children's Hospital of Pittsburgh; Dr. Walter Schiller, Cook County Hospital, Chicago; Dr. Wolfgang W. Zuelzer, Children's Memorial Hospital, Chicago; Dr. F. W. Wiglesworth, Children's Hospital, Montreal, and Dr. Archie H. Baggenstoss, Mayo Clinic.

loosely in dry borax. The remainder were shipped without borax or other preservative. On arrival at the laboratory, the tissues that were shipped in borax were freed of this substance, and when the size of the specimen permitted a small portion was removed for the preparation of slides for histopathologic study. From each parenchymal lesion tissue, suspensions were prepared for the subcutaneous inoculation of 2 guinea pigs, and the same procedure was followed with specimens of the hilar lymph nodes. In other words, each of the respective specimens was used to inoculate 2 guinea pigs.[7] In 20 cases, parenchymal lesions only were received; in 7 cases the disease was present in the hilar lymph nodes in addition to the parenchymal involvement, and in 2 instances no parenchymal lesions were received, the disease being limited to the hilar lymph nodes. Unless dying sooner, the guinea pigs were kept under observation for approximately eight weeks. At the end of this time they were killed for necropsy.

proved is summarized in table 1. The results of the animal inoculation studies for the different age groups are presented for the 29 cases shown in table 2.

The results of the animal inoculation tests when correlated with the character of the lesions from the respective cases, determined microscopically, are summarized in table 3. Unfortunately in 8 cases the amount of the tissue received was too small to permit its being divided for the preparation of sections for microscopic study. It appeared more important to utilize the entire specimen to determine the presence of viable tubercle bacilli than to divide the material in order to record the histopathologic characteristics. The morphologic character of the primary parenchymal lesion from 4 of the cases is shown in figures

TABLE 1.—*Instances in Which Viable Tubercle Bacilli Were Demonstrated in the Ghon Complex of Twenty-Nine Children Dying of Causes Other Than Tuberculosis*

Case	Age of Patient	Material		Results of Guinea Pig Inoculation	
		Lesion, Grossly	Histopathologic Data	A	B
1	2½ years	Firm nodule in lung, 0.2 cm. diameter	Two active miliary tubercles; few acid-fast bacilli present	Killed after 59 days; negative	Killed after 59 days; one nodule in spleen; culture of tubercle bacilli isolated
2	28 months	Solitary nodule in lung	No sections prepared	Killed after 59 days; extensive tuberculosis in spleen	Killed after 59 days; extensive tuberculosis in spleen
3	8 months	Solitary caseous nodule in lung	No sections prepared	Killed after 59 days; extensive tuberculosis ?	Failure; died in 12 days
4	3 years 10 months	Caseous nodule in lung, 0.1 by 0.2 cm.	Active caseous tuberculosis; acid-fast bacilli numerous	Killed after 59 days; extensive tuberculosis	Failure; died in 12 days
5	11 years	Conglomerate caseous nodules, hilar lymph nodes	Minimal calcification; active tuberculosis *	Killed after 56 days; extensive tuberculosis	Killed ofter 56 days; extensive tuberculosis

* A few discrete active miliary foci also found microscopically in one lung.

TABLE 2.—*Presence of Virulent Tubercle Bacilli in Different Age Groups in the Lesions of Primary Pulmonary Tuberculosis of Twenty-Nine Children*

Age of Patient	Number	Viable Tubercle Bacilli *	
		Not Demonstrated	Present
Less than 1 year	5	4	1
1 to 5 years	11	8	3
6 to 10 years	8	8	0
11 to 15 years	5	4	1
Totals	29	24	5 (17.2%)

* Determined by inoculation of guinea pigs.

TABLE 3.—*Infectivity of Material Representing Lesions of the Primary Complex in the Lungs and Hilar Lymph Nodes of Twenty-Nine Children*

Character of Lesions on Histologic Examination	Cases	Virulent Tubercle Bacilli
No microscopic examination	8	Positive in 2 cases; negative in 6 cases
Tuberculosis not found microscopically *	3	Negative
Caseation with encapsulation †	9	Positive in 2 cases; negative in 7 cases
Caseocalcareous	6	Negative
Mostly calcified	2	Negative
Miliary, active	1	Positive

* Material most likely to contain lesions was used for animal inoculation.

† In 3 cases, including the 2 with positive evidence of virulent tubercle bacilli, microscopic evidence of activity was shown.

RESULTS

In only 5 of the 29 cases were viable, virulent tubercle bacilli demonstrated as a result of the animal inoculation tests. Pertinent information concerning the 5 cases in which infectivity was

1, 2, 3 and 4. Of particular interest is the histopathologic character of the primary parenchymatous lesion of a 20 month old child (fig. 1). Although the center of this recently developed lesion was of a caseous character and contained no demonstrable mineral salts, portions of the

7. Attempts were also made to culture tubercle bacilli from twenty-two of the specimens, with negative results.

nodule that were used to inoculate guinea pigs failed to induce tuberculosis in either of the 2 animals.

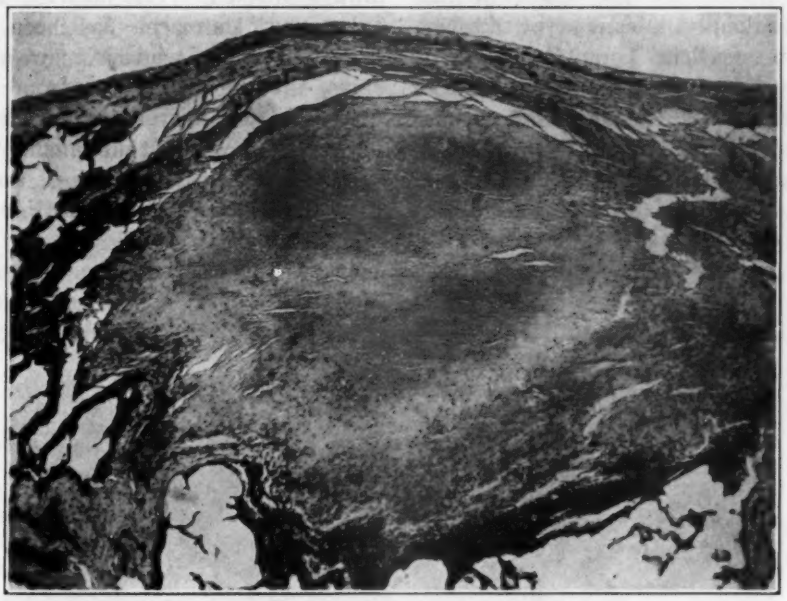

Fig. 1.—Parenchymal lesion of primary tuberculosis from a white boy 20 months of age. Note the thickened pleura and the adjacent compressed pulmonary tissue. The lesion was in the midst of a large area of fibrosis. Portions of this lesion failed to infect guinea pigs (× 43).

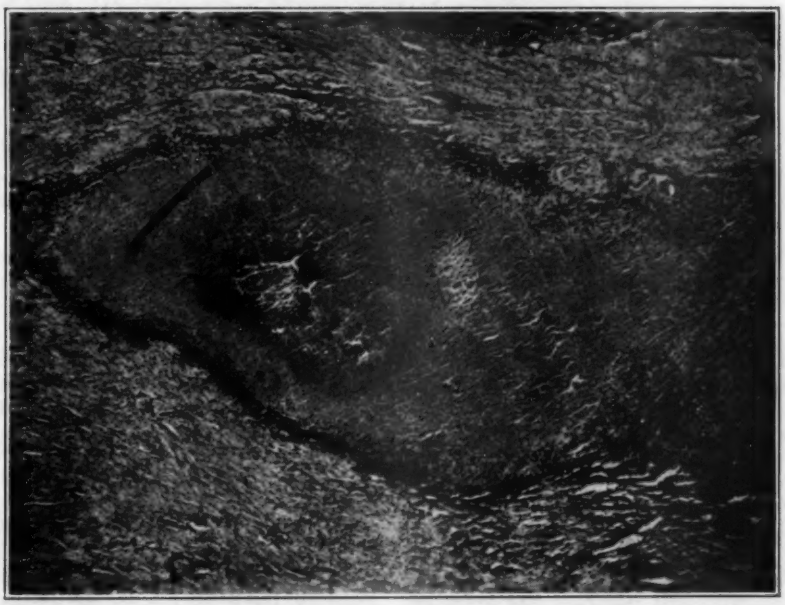

Fig. 2.—Parenchymal caseous lesion in the midst of large area of fibrosis adjacent to the primary focus. The specimen is from a 3 year old child. Material from this specimen failed to produce tuberculosis in guinea pigs (× 43).

COMMENT

The amount of material available for this study was obviously insufficient to justify more than a provisional conclusion regarding the fate of tubercle bacilli responsible for the genesis of the primary complex, especially in those instances in which the lesions are no longer progressive but instead have become encapsulated and appear microscopically to be arrested or "healed." While our group of cases is not large, it is an impressive fact that the lesions of only 5 patients (17.2 per cent) of a total of 29 patients contained demonstrable viable and viru-

lent tubercle bacilli. If, as seems likely, the primary complex in most instances tends to become sterile during the early months or years, there is, indeed, good evidence for the statement that the "prognosis in the first infective type of tuberculosis per se is excellent" [8] and that the primary infection type of tuberculosis in children is usually a benign disease when the general hygienic conditions of the environment are good. However, one should be mindful of the fact that not all lesions of the primary type in children become devoid of viable and virulent tubercle bacilli. This was true in case 4 (table 1), in which secondary tubercles occurred at the periphery of the caseous, well encapsulated primary focus (fig. 3). So long as any tubercle bacilli persist, they must be regarded as potential instigators of the reinvasion type of pulmonary tuberculosis.

Concerning the duration of a tuberculous infection when once established in a human being, it has often been said that "once tuberculous, always infected." The doctrine implied by this aphorismic statement has been generally accepted by many, who have drawn their conclusions, for the most part, from studies of the gross and the microscopic features of tuberculous lesions. Without minimizing the importance of the morphologic aspects of the pathology of tuberculosis, one must admit that, regardless of how suggestive of activity the morphologic character of a given lesion may be, one cannot say with finality whether or not the lesion, or comparable portions of it, actually contain viable virulent tubercle bacilli until the presence of the organism has been demonstrated by culture or by the inoculation of guinea pigs. Cellular reactions or other morphologic evidence of activity of a tuberculous lesion can seldom justify more than a presumption that the lesion contains viable tubercle bacilli. This is especially true of lesions that are encapsulated, fibrotic, caseous or calcified.

Fig. 3 (case 4, table 1).—Primary tuberculous focus from the lung of a child 3 years and 10 months of age. Although the parent lesion is caseous and well encapsulated, signs of activity in the contiguous tissues are evident. Note the insert in the lower right corner, which represents a higher magnification of a "daughter tubercle" in the area adjacent to the caseous primary focus. Viable, virulent tubercle bacilli were demonstrated from this specimen (× 15).

8. Myers, J. A.: The Evolution of Tuberculosis as Observed During Twenty Years at Lymanhurst (1921 to 1941), Minneapolis, Minn., The Journal-Lancet, 1944, p. 76.

It is regrettable that no knowledge is available concerning the sensitivity to tuberculin of the children in our series. Many have suggested that, as the primary complex becomes encapsulated and finally inactive or "healed," previous sensitivity to tuberculin may diminish or be lost. In our study, the failure to demonstrate the presence of living tubercle bacilli in 24 of 29 patients having childhood tuberculosis provides reasons in support of the belief that sensitivity to tuberculin in children may be transitory and that, in children whose tuberculosis is limited to the lesions of the primary complex, the continuation of the sensitivity to tuberculin is probably related to the infectivity of the tuberculous foci. It is

Norval,[10] in a recent study of 112 children with a Ghon complex, found that between a fourth and a fifth of the children did not give an intracutaneous reaction to the second strength of purified protein derivative (0.005 mg.), indicating that, as in our series of cases, in all probability there was no longer any antigen being absorbed from the tuberculous lesions and that viable tubercle bacilli were no longer present. When this is the case, it seems unlikely that tuberculosis of the adult type could develop except by reinfection. A follow-up study of such a group of cases might help determine whether such a healed infection renders a person living in a tuberculous environment refractory to the disease, produces a

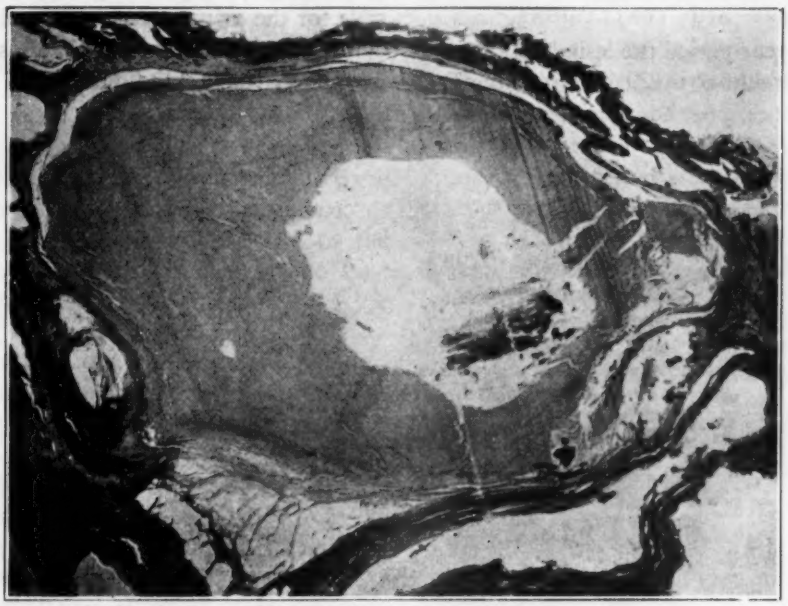

Fig. 4.—Primary parenchymal nodule from the lung of a child 13 years of age. The caseocalcareous central portion is surrounded by a thin, densely contracted capsule of connective tissue. A portion of this lesion failed to be infective for guinea pigs (× 43).

logical to assume that foci which no longer contain viable tubercle bacilli will eventually cease to contribute to the maintenance of the phenomenon of sensitivity, but the loss of this sensitivity does not necessarily indicate a loss of immunity.[9]

second primary complex or eventually produces a typical adult form of tuberculosis.

9. Rich,[1] p. 559. Recently Pottenger and Pottenger Pottenger, F. M., Jr., and Pottenger, F. M.: Disappearance of Tuberculin Reaction in Children Under Treatment for Allergies, Am. Rev. Tuberc. **47**:11 [Jan.] 43) reported the results of a study of 41 children who experienced a reversal of their sensitivity to tuberculin while being treated for bronchial asthma, hay fever, bronchitis and "low energy and delayed development." The treatment was largely dietetic, the patients receiving a diet rich in protein and animal fats and relatively low in carbohydrates. The diet was supplemented with enerous amounts of vitamins, obtained largely from atural sources, and with an extract from the adrenal ortex. The authors expressed the belief that the reaction in sensitivity to tuberculin observed in their study was due to an enhancement of the mechanism of resistance as a consequence of the improved physiologic state resulting from the prescribed dietary regimen. While this report constitutes a highly interesting clinical observation, it lacks persuasive experimental evidence in support of the premise that in children the continuation of sensitivity to tuberculin is related to a nutritional deficiency and that the correction of this dietary unbalance will result in a disappearance of the sensitivity to tuberculin. A proper control series of comparable patients would seem exceedingly important in studies of this sort. Furthermore, cognizance should be taken of the probable dependence of the sensitivity to tuberculin of diagnostic significance on the persistence of viable tubercle bacilli within the body of the person with a positive reaction to tuberculin.

10. Norval, M. A.: Tuberculin Reaction in Children with a Ghon Complex: Review of One Hundred and Twelve Cases, Am. J. Dis. Child. **70**: 1 (July) 1945.

There remains the question whether from this study any evidence can be deduced that will shed any light on the relationship of the Ghon tubercle to the adult type of tuberculosis. If, as shown in 24 of the cases, the lesions contained no viable tuberculosis bacilli, then naturally they could not be the cause of further tuberculous involvement. But if, on the other hand, as in figure 3, active "daughter tubercles" were still present, then the adult type of the disease might develop. Undoubtedly, the general hygienic condition of the patient may be responsible for the more complete healing of primary tuberculosis, both through the increased individual resistance and through the decreased size of the infecting dose.

SUMMARY AND CONCLUSIONS

During a six year period the lesions of primary pulmonary tuberculosis in 29 children dying of causes other than tuberculosis were examined for the presence of virulent tubercle bacilli. Each specimen was used to inoculate 2 guinea pigs and the results were observed at necropsy eight weeks later. In only 5 of the 29 patients were virulent tubercle bacilli demonstrated. The youngest child in whom virulent tubercle bacilli were found was an infant of 3 months, and the oldest in whom the results were positive was a child of 11 years.

If the results of the study of this small series of cases are a true reflection of the state of infectivity of the lesion of the primary complex in children without concomitant tuberculous disease, one may conclude that the tubercle bacilli responsible for the primary lesions of pulmonary tuberculosis of childhood tend in most instances to become avirulent or to disappear.

STUDIES ON THE STREPTOCOCCI ("ENTEROCOCCI") OF LANCEFIELD GROUP D

II. RECOVERY OF LANCEFIELD GROUP D STREPTOCOCCI FROM ANTEMORTEM AND POSTMORTEM CULTURES FROM INFANTS AND YOUNG CHILDREN

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Numerous reports have been published recently on infections associated with streptococci of serologic groups other than Lancefield group A.[1] In general, infections with non–group A streptococci are considered rare or atypical in cases of diseases of the respiratory tract, such as scarlet fever and tonsillitis. On the other hand, non–group A streptococci are found frequently with urinary and puerperal infection.[2] Postmortem cultures may reveal such organisms in cases of terminal infection. In certain of these cases the presence of a particular streptococcus is of questionable significance, the site of the lesion and the lowered resistance of the host having more to do with the infection than the "virulence" of the micro-organism.

However, enough observations have accumulated to indicate the importance of non–group A streptococci in human infection and to warrant reexamination of the rather rigid interpretation which the clinician, on the advice of the bacteriologist, has become accustomed to assign to serologically grouped streptococci isolated from infected persons. It is not intended to dispute the general correlation of group A streptococci with human disease but, rather, it is our purpose to point out the potential pathogenic significance of certain of the other groups of streptococci which, although ordinarily harmless saprophytes, may produce disease in the human host if provided with the proper conditions.

The group D streptococci appear to belong to this class of micro-organisms and seem, under certain conditions, to be of pathogenic significance. One of these conditions appears to be the early age of the host. Carrier studies and cultures of material taken from lesions in infants in wards and at the autopsy table revealed that group A streptococci were not the only streptococci carried by these infants or group A the only serologic group associated with disease in these patients. Cultures of material from the throats of infants in the neonatal period indicated that while beta streptococci were occasionally present in the throat, these streptococci often did not belong to group A. The present study is concerned with the presence of group D streptococci in cultures of material from the throats of infants suffering from infections of the upper respiratory tract and in cultures of material taken post mortem from infants and young children.

TABLE 1.—*Blood Agar Reaction and Serologic Group of Streptococci Isolated from Cultures of Material from Throat and Rectum of 24 Babies from Well Baby Clinic, Aged 9 Weeks to 2 Years*

Streptococci Isolated		Source		Blood Agar Reaction		
Group	Type	Throat	Rectum	Alpha	Beta	Gamma
A	1	1	..	..	1	..
A	24*	1	..	..	1	..
A	28	1	..	..	1	..
D	H 69 D6	..	8	3	..	5
D	Lanc. 1	..	2	..	1	1
H	..	1	..	1	..	..
K	..	1	..	..	1	..
Streptococcus viridans †.....		23‡	..	22	..	1
Total strains.....		28	10	26	5	7

* Weak cross agglutination with types 4, 19, 26 and 29.
† Classification of "Streptococcus viridans" throughout this paper is made on the basis of failure of extracts to react with rabbit antiserums for Lancefield groups A through M.
‡ All alpha colonies fished were insoluble in bile.

OBSERVATIONS

Strains Isolated from Well Babies.—Table 1 shows the results of carrier studies on infants

† Lieutenant Wheeler was killed in action on April 13, 1945.

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writers and are not to be construed as reflecting the policies of the Navy Department.

1. Rantz, L. A.: Streptococcal Meningitis: Four Cases Treated with Sulfonamides in Which the Etiological Agent Was an Unusual Streptococcus, Ann. Int. Med. **16**:716, 1942. Wheeler, S. M., and Foley, G. E.: A Note on Non-Group A Streptococci Associated with Human Infection, J. Bact. **46**:391, 1943.

2. Fry, R. M.: Fatal Infections by Hemolytic Streptococci Group B, Lancet **1**:199, 1938. Porch, M. A.: Bacteriological Study of the Streptococci Isolated from the Urinary Tract, J. Bact. **41**:485, 1941.

seen in a well baby clinic. The strains cultured were classified according to a technic previously described.[3] Two inferences can be drawn from this small series: First, whatever the pathogenesis of group D streptococci, they are found most frequently in the flora of the gastrointestinal tract, and, second, beta reactions on blood agar are not a constant characteristic of these streptococci. Failure to appreciate the latter fact invalidated many earlier and more extensive attempts to determine the normal incidence of the various serologic groups of streptococci in healthy infants.

Strains Isolated from Infants with Infections of the Respiratory Tract.—In the spring of 1941 an outbreak of mild disease of the upper respiratory tract (essentially a purulent rhinitis) occurred in the premature baby nursery and the private nursery of a local lying-in hospital. Cultures of material from the throat revealed a heavy growth of beta streptococci among infants suffering from the infection and among infants in contact with them as well. Serologic studies of several of the strains showed them to belong to Lancefield group D, type H 69 D5.[3] These micro-organisms were not heat resistant and did not survive pasteurizing temperature in milk or formulas. Epidemiologically, the mode of spread suggested respiratory, and possibly air-borne, transmission. In December beta streptococci were again noted in the throats of a few infants with mild disease of the upper respiratory tract and in the throats of infants in contact with them. In another institution, several babies were observed to be carrying this micro-organism in August 1942, but at that time the presence of the organism was not associated with an unusual incidence of infection. In the winter of 1942-1943 and again in the spring of 1943 this streptococcus was associated with infection of the upper respiratory tract and diarrhea respectively in the nurseries of the same institution. Detailed epidemiologic and clinical studies of the outbreaks occurring in 1943 again suggested, but did not establish, respiratory and possibly airborne transmission.[4] Except in these instances, large numbers of group D streptococci have not been observed in cultures of the material from the throats of infants and newborn babies.

TABLE 2.—*Serologic Classification of Streptococci Isolated from Throat Cultures of Living Infants*

Series	Diagnosis	No. of Cultures	Streptococci Isolated		Serologic Classification: Group O	Group D: H 69 D5	Group D: Lanc 1	Group D: Lanc 3	Group D: D76	Group D: Untyped*	Group H	Unclassified
Hospital A	Infection of upper respiratory tract †	102	Alpha	21	..	13	3	..	..	..	3	2‡
			Beta	17	..	8	2	..	..	7		
			Gamma	34	1	1	..	..	..	..	..	32
Hospital B	Infection of upper respiratory tract †	89	Alpha	8	..	4	..	..	..	..	..	4‡
			Beta	58	2	46	1	..	..	8	1	
			Gamma	4		..	..	..		..	..	4
Hospital C	Infection of upper respiratory tract †	21	Alpha	3	..	3						
			Beta	18	..	17	1					
			Gamma									
			Alpha	32	..	20	3	..	..	..	3	6‡
			Beta	93	2	71	4	..	..	15	1	
			Gamma	38	1	1	..	..	..	..	..	36
Total		212		163	3	92	7	..	..	15	4	42
Controls	Well babies (hospitals B and C)	120	Alpha	58	..	3	..	..	..	..	1	51‡
			Beta	8§	..	1	1	..	..	1		
			Gamma	34	..	5	1	..	..	1	..	27
Total		120		97	9	2	..	..		2	1	78

* Classified before type serums became available.
† Data for both sick infants and for infants in contact with them.
‡ Streptococcus viridans.
§ Includes three group A and two group K strains.

The results of studies on this series of streptococcus cultures are summarized in table 2. A comparison of the serologic groups encountered among infants with infections of the respiratory tract and those isolated from well babies in the same institutions indicates that, although streptococci were frequently found in both series, the majority of strains isolated from sick infants, irrespective of their appearance on blood agar, belonged to group D (table 2).

Strains Isolated from Adults.—The epidemiologic relationship of group A streptococci

3. Foley, G. E., and Wheeler, S. M.: Studies on the Streptococci ("Enterococci") of Lancefield Group D: I. Serologic and Biochemical Characteristics, Am. J. Dis. Child. **70:** 93 (Aug.) 1945.

4. Dr. C. G. Jennings, formerly of Children's Hospital, provided the clinical and epidemiologic data relating to these outbreaks.

streptococcic infection of the respiratory tract in adults is well established.[5] There is reason to believe that similar relationships do not always hold for the streptococci involved in such infections in infants and young children. Although group D streptococci have occasionally been isolated from infected adults[1] the experience in this laboratory and elsewhere[6] has been that group D streptococci (especially those with the beta reaction on blood agar) are seldom present in the throats of adults. Table 3 shows the serologic classification of the few group D strains (exclusive of those associated with subacute bacterial endocarditis) which have been isolated from adult carriers and infected persons in this laboratory.

Postmortem Cultures.—During the past two and one-half years the streptococci isolated at autopsy have been classified serologically. During this period strains isolated at autopsy on 67 infants and young children have been studied sufficiently to warrant analysis.[7] Table 4 summarizes some of the data most pertinent to these sources, together with data from 6 cases from other sources. As will be seen from the table,

TABLE 3.—*Serologic Classification of Group D Streptococci Isolated from Adults* **

Diagnosis	Source	No. of Strains	Blood Agar	Heat Resistance	Serologic Type
Normal carriers †	Throat	5	Alpha	—	H 69 D5
Postvenereal infection of urinary tract	Urine	15	Alpha	—	H 69 D5
Cervical adenitis	Drainage	1	Alpha	—	H 69 D5
Pleurisy	Thoracic fluid	3	Gamma	—	H 69 D5
Chronic tonsillitis	Excised tonsils	1	Beta	—	H 69 D5
Cystitis	Catheterized urine	3	Alpha	+	Lanc 3
Mastoiditis	Drainage	1	Alpha	—	? ‡

* Exclusive of patients with subacute bacterial endocarditis.
† Less than 0.1 per cent of the total number of strains studied.
‡ Probably Str. viridans.

the subjects ranged from newborn infants to young children, none being over 11 years of age. Ninety-four strains of streptococci were isolated from these subjects. Table 5 summarizes the serologic classification and the cultural characteristics of these strains on blood agar, as well as the anatomic sources from which they were isolated. Of the strains isolated, 61 (65 per cent) were group D streptococci. When these organisms were isolated they were obtained in pure culture or in predominant numbers at 47 (79 per cent) of the autopsies (table 6). There was no constant correlation between the presence of group D streptococci and that of other organisms, the organism most frequently encountered with streptococci being Staphylococcus aureus, which was isolated at 11 (18 per cent) of the autopsies. Certain characteristics of the serologic types of group D streptococci encountered in antemortem and postmortem cultures from infants and young children are summarized in table 7, together with characteristics of a few strains isolated from other sources. It appears that potentially pathogenic bacteria, such as Staph. aureus, Escherichia coli and, in the instances recorded here, group D streptococci, frequently are capable of invading the infant host, especially if the resistance of the host is altered by concurrent infection, malformation, nutritional deficiency or other condition leading to debilitation.

TABLE 4.—*Diagnosis and Age Distribution for 73 Children Examined at Autopsy for Streptococci*

Diagnosis	No. of Children	Age
Pulmonary disease	14	13 hr. - 7 yr.
Congenital malformation	10	6 days - 2 yr.
Blood dyscrasia	8	5 days - 7 yr.
Encephalitis and hydrocephalus	6	2 mo. - 2 yr.
Abdominal disease	5	9 days - 6 wk.
Sepsis	5	11 days - 3 yr.
Brain abscess	4	1 mo. - 6 yr.
Tracheitis	3	7 mo. - 13 mo.
Other disease *	18	Newborn - 11 yr.

* Sudden, unexplained death; nephritis; tuberculous meningitis; acidosis; otitis media; diarrhea; rheumatic fever; glycosuria; encephalitis complicating measles; Ritter's disease; Tay-Sachs disease.

Strains Isolated from Infants with Acute Fulminating Infections with Fatal Outcome.—The importance of the streptococcus as an important cause of sudden, unexplained death in early life was emphasized by Farber.[8] In the series of 73 deaths considered in this study, 22 (30 per cent) were considered unexpected, since they occurred early in the primary illness. Of the 28 strains of streptococci isolated from patients whose deaths fall in this category, 24 (86 per cent) belonged to group D. The source and serologic characteristics of all the streptococci isolated from these patients are considered in table 8. It would appear from these observations that, although group D streptococci are frequently encountered in patients with this type of infection, the ability

5. Schwentker, F. F.; Janney, J. H., and Gordon, J. E.: The Epidemiology of Scarlet Fever, Am. J. Hyg. 38:27, 1943.

6. Rantz, L. A.: The Hemolytic Streptococci: Observations on the Carrier State in the San Francisco Area, J. Infect. Dis. **69**:248, 1941.

7. Dr. Sidney Farber, pathologist, Children's Hospital, provided the autopsy material used in this study.

8. Farber, S.: Fulminating Streptococcus Infections in Infancy as a Cause of Sudden Death, New England J. Med. **211**:154, 1934.

to produce fulminating infections is not confined to any single species of streptococcus—most likely the production of such infections depends on factors of resistance in the infant host, which are frequently seen to permit invasion and establishment of septic foci with a minimum of detectable clinical response. The association of these organisms with certain pathologic changes will be reported later by Dr. Sidney Farber.

COMMENT

That "enterococci" may at times be etiologically related to disease in man was first observed by Andrews and Horder.[9] Accurate interpretation of the older literature on "enterococcic" infection is difficult, in view of the numerous, and often unreliable, differential tests employed for identification of the organisms. The development of the group precipitation technic[10] and the separation of group D streptococci into serologic types provide an accurate method of recognition, as well as an epidemiologic tool for the kind of study reported here. Certain biochemical characteristics[3] are valuable in recognition of group D streptococci in the absence of serologic examination but are of little value in differentiation of types. In any case, complete dependence on biochemical activity alone may result in failure to

TABLE 5.—*Serologic Classification of Streptococci Isolated from Cultures Made Post Mortem: Anatomic Source and Blood Agar Reactions*

Source	No. of Cultures	Blood Agar Reaction	Serologic Classification: Group A	Group B	Group C	Group D: H 69	Group D: D5	Group D: Lanc 1	Group D: Lanc 3	Group D: D76	Group E	Group H	Group K	Unclassified*
Heart blood	34	Alpha	..	1	..	10	5	2	..	..	..	..	4
		Beta	..	2	1†	3	1	..	1	..	1		
		Gamma	..	1	..	1	..	..	..	..	1		
Lungs	42	Alpha	..	..	..	4	10	2	..	1	..	..	7
		Beta	1‡	4	..	3	1	3	..	..	1		
		Gamma	..	..	..	1	1	1	..	..	1	..	1
Trachea	3	Alpha	..	..	..	..	1						
		Beta	..	..	..	..	1						
		Gamma	..	..	..	..	..	..	..	..	1		
Brain	3	Alpha	..	..	..	..	2						
		Beta											
		Gamma	..	..	..	1							
Other sources§	12	Alpha	..	1	..	2	3	..	..	..	..	1	
		Beta	1‖	2	..	..	1						
		Gamma	..	..	..	..	1						
Total	94		2	11	1	25	27	8	1	1	5	1	12
Percentage			2	11	1	27	29	8	1	1	6	1	13

* Includes strains classified as "Str. viridans" and three strains not studied
† Human type (ferments trehalose).
‡ Griffith type 19 (weak cross agglutination with types 4, 24, 26 and 29).
§ Includes 2 cultures of the spinal fluid, 2 of ears, 1 of exudate, 4 of intestinal material and 3 miscellaneous cultures.
‖ Griffith type 1.

TABLE 6.—*Group D Streptococci: Predominance of 61 Strains Recovered at Autopsy*

Proportion of Group D Streptococci		No. of Cultures (Autopsy)	Per Cent
Pure culture		24	39.2
Predominant		23	42.5
With Staph. aureus	6		
With other micro-organisms*	17		
Few		14	21.3
With Staph. aureus	5		
With other micro-organisms*	9		
Total		61	
Pure culture	24		
With Staph. aureus	11		
With other micro-organisms	26		

* In this order of frequency: Esch. coli, Bacillus proteus, Bacillus alcaligenes (Alcaligenes fecalis), Bacillus pyocyaneus, Streptococcus albus, Micrococcus flavus, and 1 each of Pneumococcus and Streptothrix.

recognize some strains of group D or in confusing some strains of other serologic groups (group E especially) with strains of group D. The identification of strains such as those considered here as members of Lancefield group D may be of diagnostic importance, in view of the well established resistance of group D streptococci to sulfonamide chemotherapy.[11]

As was pointed out by Lancefield,[12] the correlation of serologic group with hemolytic ac

9. Andrews, F. W., and Horder, T. J.: A Study of the Streptococci Pathogenic for Man, Lancet **2**:708, 775 and 852, 1906.

10. Lancefield, R. C.: A Serological Differentiation of Human and Other Groups of Streptococci, J. Exper. Med. **57**:571, 1933.

11. Neter, E.: The Bacteriostatic Action of Sulfonamides upon Hemolytic and Nonhemolytic Enterococci, J. Bact. **40**:383, 1940.

12. Lancefield, R. C.: Specific Relationship of Cell Composition to Biological Activity of Hemolytic Streptococci, in Harvey Lectures, 1940-1941, Baltimore, Williams & Wilkins Company, 1941, vol. 36, p. 251.

vity is not so strict as was supposed. The riginal classification of serologic groups was estricted to streptococci producing beta reac-ions on blood agar, but it has become apparent hat non-beta strains occur among the various erologic groups. This is especially true of the roup D streptococci, among which alpha, beta

definition of the term. As was pointed out previously,[8] neither serologic type nor source of culture could be correlated with reaction on blood agar or biochemical activity.

The ubiquity as well as the instability of biochemical and physiologic characteristics of the alpha streptococci has often obscured the correct

TABLE 7.—*Serologic Classification of Group D Streptococci from All Sources: Reaction on Blood Agar and Resistance to Heat*

Source	No. of Strains		H 69 D5				Lanc 1				Lanc 3				D76				Untyped *			
			Reaction on Blood Agar		Heat Resistance		Reaction on Blood Agar		Heat Resistance		Reaction on Blood Agar		Heat Resistance		Reaction on Blood Agar		Heat Resistance		Reaction on Blood Agar		Heat Resistance	
			No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Throat cultures, living infants	127	Alpha	23	23	2	9	3	33	1	33	..	..	..	..	..	..	..	..	15	100	?	?
		Beta	72	71	2	9	5	56	1	20	..	..	..	..	..	..	..	..	..	..	..	..
		Gamma	6	6	..	..	1	11	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Postmortem cultures, infants	61	Alpha	16	60	2	12	21	78	5	23	4	44	..	..	..	..	..	..	..	..	..	..
		Beta	6	26	..	..	4	14	2	50	3	33	1	11	1	..	1	..	..	..	..	..
		Gamma	3	5	..	..	2	7	1	50	1	12	..	..	..	..	..	..	..	..	..	..
Miscellaneous cultures, adults and well babies	39	Alpha	27	84	..	..	..	..	..	..	3	60	3	..	1	..	1	..	..	..	..	..
		Beta	1	3	..	..	1	..	..	..	2	40	..	..	..	..	..	..	1	..	?	?
		Gamma	4	12	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	?	?
Total	227		158		6		37		10		13		4		2		2		17		?	?
Per cent			70		4		16		3		6		30		1		100		7			

* Of the 210 strains tested, 29 (10.2 per cent) were heat resistant. If the 17 strains not tested were assumed to be heat resistant, then 17 per cent of the strains would have the characteristic usually associated with "enterococci." These strains were grouped before type serums became available.

nd gamma strains were encountered. None of he strains produced soluble hemolysin; hence ven those producing beta reactions on blood gar are not hemolytic streptococci by the strict

TABLE 8.—*Serologic Classification of 28 Strains of Streptococci Isolated Post Mortem from 22 Infants and Young Children Whose Deaths Were Considered Sudden and Unexpected*

Patient	Source of Culture	Blood Agar Reaction	Heat Resistance	Serologic Group	Classification Type
1	Blood	Beta	—		
2	Blood	Alpha	—		
3	Blood	Alpha	—	D	H 69 D5
4	Blood	Beta	+		
5	Blood; lung	Alpha	—		
6	Blood	Aluha	+		
7	Blood	Alpha	—	D	Lanc 1
	Brain	Alpha	—	D	Lanc 1
	Brain	Gamma	—	D	H 69 D5
8	Blood	Alpha	—	D	H 69 D5
	Colon *	Alpha	—	D	Lanc 1
9	Blood	Beta	—*	C	Human †
	Lung	Alpha	—	D	H 69 D5
10	Lung	Beta	—		
11	Peritoneum	Beta	+		
12	Lung	Alpha	—		
13	Blood; lung	Alpha	+		
14	Spinal fluid	Beta	—	D	Lanc 1
15	Blood	Gamma	+		
16	Lung	Alpha	—		
17	Lung	Alpha	—		
18	Colon ‡	Alpha	—		
19	Brain	Alpha	—		
20	Lung	Alpha	—		
21	Trachea	Beta	—	H	
22	Trachea	Alpha	—		

* Present in pure culture.

† Ferments trehalose; does not ferment sorbite.

‡ Predominant micro-organism.

identification of these strains and has invalidated various attempts to determine their exact pathogenic significance. The recovery of such organisms from infected persons has been observed frequently, but until recently [13] little attempt has been made to determine their correct identity (or diversity) on a serologic basis. In general, the same is true of the "enterococci." Although alpha, beta and gamma strains exist in this group of organisms, resistance to heat was long thought to be a distinguishing characteristic of the entire group. A relatively small percentage of the strains reported here possessed this property (table 7). Heat-resistant strains were encountered in all serologic types of group D streptococci, and this characteristic could not be correlated with the sources of culture.

Although their exact pathogenesis is as yet unknown, streptococci identified serologically as members of group D are frequently isolated from infected persons. Rantz and Kirby [14] reported 145 cases in which group D streptococci were isolated from various sources. The general impression that the "enterococcus" is the usual species involved in streptococcic infections of

13. Soloway, M.: A Serological Classification of Viridans Streptococci with Special Reference to Those Isolated from Subacute Bacterial Endocarditis, J. Exper. Med. **76**:102, 1942.

14. Rantz, L. A., and Kirby, W. M. M.: Enterococcic Infections, Arch. Int. Med. **71**:516 (April) 1943.

the urinary tract is supported by the studies of Rantz [15] and Porch.[16] The presence of group D streptococci in cultures of the blood from patients with subacute bacterial endocarditis also is well established.[14] Werne [17] reported the isolation of group D streptococci from patients with acute, fulminating infections similar to those considered here.

In the present study the isolation of group D streptococci from cultures of material from the throat of infants with purulent rhinitis and from infants in contact with them suggested a causal relationship between these organisms and infection of the respiratory tract and an air-borne, person-to-person mode of spread. On the other hand, the recovery of group D streptococci from postmortem cultures of body tissues and fluids of infants was considered a result of invasion by these organisms from sources in their natural habitat, the gastrointestinal tract. It is well established that bacterial invasion of the blood stream, the lungs and the meninges is frequently encountered in cases of terminal infection in infants and that such septic conditions are usually accompanied with a minimum of symptomatic response on the part of the host. It has been suggested that babies are susceptible to such infections because they have not yet acquired immunity in the form of specific antibodies to these organisms. It is also possible that the young infant is more susceptible than older persons to bacterial invasion because of anatomic and physiologic differences in the very young, which may allow the organisms to migrate the length of the alimentary canal or to penetrate the mucosal layers with relative ease. It cannot be said without further observation that group D streptococci are a primary cause of death in infants. Neither are the observations recorded here intended to imply that group A streptococci are negligible as a cause of disease and death in this age group; one outbreak of acute, fulminating infection among newborn infants (omitted from the tables because of lack of complete data) was associated with presence of a group A, Griffith type 25 hemolytic streptococcus.

Although serologic classification is invaluable to the diagnostic and epidemiologic aspects of the problem of streptococcic infection, it becomes increasingly evident that the common physiolog factor, measured by serologic technics, represen but a portion of a complex cellular biology. I deed, the correlation of pathogenicity with ser logic group is not so clearcut as is supposed- a fact which in itself suggests the existence some broad basis for the ability to produce di ease regardless of serologic characteristics. Th age distribution of patients from which group streptococci were isolated in this study and that of Rantz and Kirby,[14] together with th relative infrequency with which group D stre tococci are isolated from the adult, draws atte tion to variables in the host as a factor in t ability of a given streptococcus to produce di ease. The physiologic characteristics of the ho and fluctuations induced in resistance of the ho may be more important than the micro-organis in determining the result of exposure to infectio This emphasis on factors in the host implies t necessity for caution against conclusions made terms of specific infecting parasites. The resul recorded here suggest, but do not prove, su specificity, the proper interpretation being th group D streptococci appear to cause trouble the proper circumstances in certain restrict age groups.

SUMMARY

Streptococci belonging to Lancefield group were isolated by culture of material from t nose and throat of infants (and of infants in co tact with them) during three separate outbrea of mild disease of the upper respiratory tra (essentially a purulent rhinitis) and one outbre of diarrhea. Detailed epidemiologic and clinic studies suggested, but did not establish, respir tory, or possibly air-borne, transmission.

Studies on well babies indicate that in the i fant the natural habitat of these organisms is t gastrointestinal tract. Beta characteristics a not specific for this group of streptococci—a f which invalidates many earlier and more exte sive attempts to determine the incidence of t various serologic groups of streptococci in norm infants.

During the period of this study 94 strains streptococci were isolated at autopsy from infants, who died from various causes. Of the strains, 61 (65 per cent) belonged to Lancefie group D. All four serologic types within gro D were encountered in this series; there was correlation between serologic type and clini diagnosis or source of culture. Neither was th any constant relationship between the presence group D streptococci and that of other orga isms; Staph. aureus was encountered frequen but not consistently.

15. Rantz, L. A., in Steele, J. M., and others: Advances in Internal Medicine, New York, Interscience Publishers, Inc., 1942, vol. 1, p. 137.

16. Porch, M. L.: Bacteriological Study of the Streptococci Isolated from the Urinary Tract, J. Bact. **41**:485, 1941.

17. Werne, J.: Postmortem Evidence of Acute Infection in Unexpected Death in Infancy, Am. J. Path. **18**:759, 1942.

Of the 73 deaths, 22 (30 per cent) were considered sudden and unexpected; they occurred early in the primary illness, as the result of acute, fulminating infection. Twenty-eight strains of streptococci were isolated from the patients who died suddenly. Although it appeared that the ability to produce such infections was not confined to any single group of streptococci, 24 (86 per cent) of the strains isolated were of one or the other of the two commonest types (H 69 D5 and Anc 1) in group D.

It would seem that under proper conditions group D streptococci may be of pathogenic significance. One of these conditions appears to be the age of the host. Group D streptococci frequently invade the infant host, especially if resistance of the host is altered by concurrent infection, malformation, nutritional deficiency or other factors leading to debilitation. Additional factors may be the lack of antibodies against these organisms and the anatomic and physiologic differences between the infant and older children or adults. Differences in the host are further emphasized by the relative infrequency with which group D strains are isolated from infected adults. Although Group A streptococci can and do produce serious infection in the infant host, it appears that the well established relationship of group A to infection in the older age groups does not necessarily hold for the infant host.

Alpha, beta and gamma strains were encountered in all serologic types of group D streptococci. None of the strains produced soluble hemolysin or erythrogenic toxin. The majority of strains were avirulent for mice, and relatively few (10 per cent) were resistant to heat.[3] Biochemical characteristics were of no value in the recognition of the various serologic types.

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NUTRITION STUDIES ON CHILDREN LIVING AT HOME

I. CALORY INTAKES ON THE BASIS OF AGE FROM ONE THROUGH TEN YEARS

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This paper is the first of a series dealing with the dietary intakes and eating habits of a group of well children living at home under conditions which are representative of a middle class population in the Boston area. The material presented has been collected over a period of fifteen years as a part of the research program on growth and development of the well child conducted by the Department of Maternal and Child Health of the Harvard School of Public Health. Three hundred and twenty-four children have been enrolled, and approximately 160 of these are still being studied. A detailed description of the studies under this program has been given in another publication.[1]

This paper deals with the average calory intakes of these children from 1 through 10 years of age. Nutritional histories were taken from the mothers by trained nutritionists in conjunction with routine clinic examinations of the children at six month intervals.[2] In addition, the mothers recorded on forms designed to allow a minimum of omissions the food consumed during a consecutive three day period, usually near to the clinic visit. Two forms have been used for each nutritional history: one to provide a detailed record of the food intake for the twenty-four hour period preceding the clinic visit and the other to record general information and to provide a picture of the average, or usual, dietary habits of the child.

Under general information are recorded the usual times of meals and of eating between meals, appetite, general attitude toward food and any special food likes or dislikes. The average daily or weekly intake lists separately such foods as milk, cheese, eggs, lean meat, fish, liver, poultry, prepared meats, fruits and vegetables, butter and other fats, cereals and breads, macaroni and spaghetti. The amounts of crackers, cookies, cake, pie, puddings, ice cream, candy and other sweets usually eaten by the child are recorded, as well as information as to the use of cocoa, chocolate syrup, tea, coffee and soft drinks. Data are also collected concerning the use of cod liver oil, or a substitute, and other vitamin or mineral concentrates. The number of persons in the family, the amounts of food purchased, the amount of money spent for food each week and other related information are considered. This method of cross checking the different records obtained has been found to contribute greatly to the accuracy of the final dietary estimates. Samples of forms used in taking these nutritional histories and further details are given in two early publications.[3]

The calory values used in the calculation of these diets were based on several standard tables of food values,[4] and the values used are as representative of those currently accepted as

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This study was begun under a grant from the General Education Board of The Rockefeller Foundation and is being continued under a grant from the James Foundation. The nutrition studies have been supported in part py a grant from the Forsyth Dental Infirmary, Boston.

1. Stuart, H. C., and others: Studies from the Center for Research in Child Health and Development, School of Public Health, Harvard University: I. The Center, the Group Under Observation, Sources of Information, and Studies in Progress, Monographs of the Society for Research in Child Development, National Research Council, Washington, D. C., vol. 4, no. 1, 1939.

2. The children were examined at six month intervals within a definite number of days of their yearly and half yearly birthdays, the variation allowed increasing from plus or minus one week at 1 year of age to plus or minus one month at 10 years, in order that all data should be representative of equivalent age periods for comparative study.

3. Burke, B. S., and Stuart, H. C.: A Method of Diet Analysis, J. Pediat. **12**:493-503 (April) 1938. Stuart and others.[1]

4. Bowes, A. deP., and Church, C. F.: Food Values for Portions Commonly Used, Philadelphia Child Health Society, 1944. Taylor, C. M.: Food Values in Shares and Weights, New York, The Macmillan Company, 1942. Rose, M. S.: A Laboratory Handbook for Dietetics, ibid., 1937. Tables of Food Composition Giving Proximate, Mineral and Vitamin Components of Foods, Based on N. R. C. Army Tables, Committee on Food Composition of the Food and Nutrition Board, National Research Council, Washington, D. C., Nov. 1, 1943.

ossible. When changes have been made in values owing to newer knowledge, corrections have been made in earlier calculations so that uniform values apply throughout. Since nutritional histories were taken at six month intervals, the calory value of the diet at nineteen age levels is available. The data include dietary intakes of 269 children, of whom 128 are boys and 141 girls. The total number of calory intakes included in this series is 5,916, of which 3,128 are of boys and 2,788 of girls. No data for children under 1 year of age are given because many of the infants

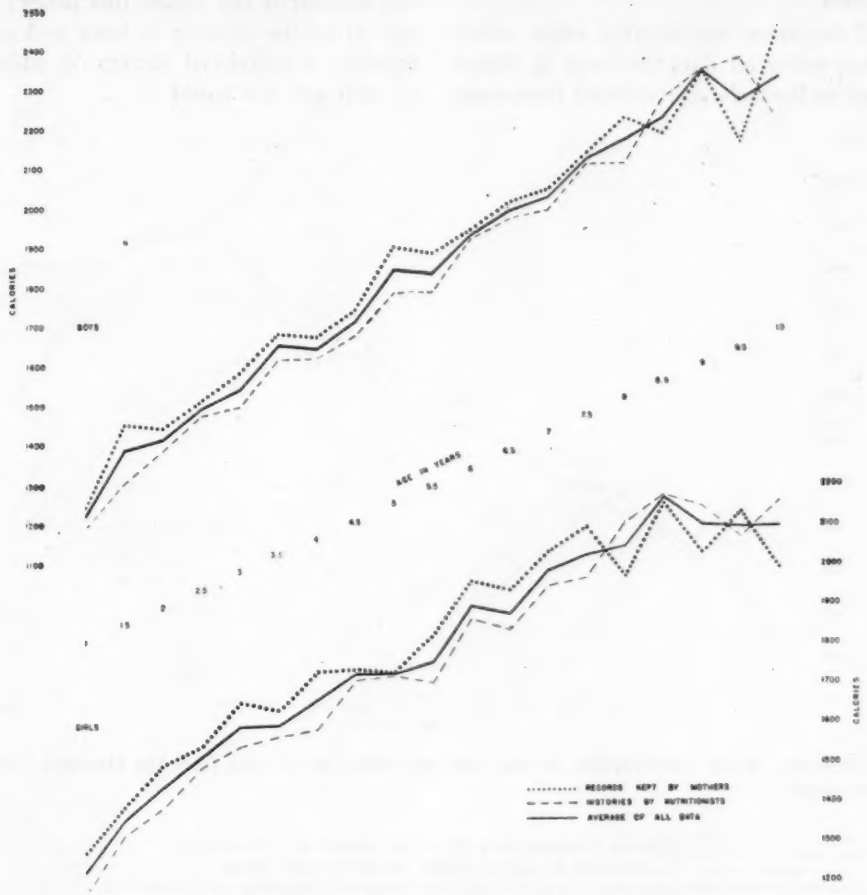

Chart 1.—Average calory consumption by age.

were breast fed for a part of this period and the information as to the amounts of nourishment obtained is not sufficiently detailed to warrant computation on a calory basis. Also, variation in requirements month by month in the first year of life would necessitate analysis of the material on that basis. It is planned to deal in subsequent papers with relationships between the calory intakes of these children and their growth and development and also with the dietary intakes of essential nutrients at each age level.

The mean calory intake for age as given in Chart 1 represents (1) the average calory value of the daily intakes calculated from the histories obtained by the nutritionists, (2) the average calory value of the dietary intakes recorded by the mothers for consecutive periods within the age interval and (3) the average of all data, which included (1) and (2). We are inclined to believe that this last value, the average of all data, is the most representative and tends to eliminate errors of possible underestimation or overestimation in individual intakes. One should also consider that the large number of intakes recorded tends to cancel out the errors due to variations in daily consumption of food by any child, as well as errors in history taking and evaluation.

It is apparent from chart 1 that in both sexes until 7½ years of age the average calory values of the intakes recorded by the mothers are consistently higher than those obtained from the nutritionists' histories, whereas at 8 years and after they tend to be lower. The differences at the earlier ages may be due to a tendency of the mothers to overestimate the amounts of food consumed or to an attempt by the nutritionist to be

conservative in her estimates or possibly to greater difficulty in estimating the calory value of some of the foods in the records kept by the mothers. After 7½ years the mother finds it increasingly difficult to tell accurately what the child eats, especially what is eaten between meals or away from home. We have established sufficiently good relationships with these children over a long period to obtain this information to supplement the mother's history directly from them. We believe that after this age the best history is obtained by questioning both the mother and the child.

In chart 2 the curve representing mean calory intake for age using all data for boys is shown superimposed on the curve constructed from comparable values for girls. It is apparent from the curves that there is little difference between the mean calory intake of boys and girls until approximately 5 years of age. The values for the boys are found to be consistently higher at all subsequent ages reported here. This difference is logical when one considers the greater activity of the average boy of school age in comparison with the usual activity of a girl of the same age. The table gives the mean calory values for age and sex, using all data, and the standard deviation range (two thirds of the values in any group will ordinarily fall within this range). This table also gives the number of boys and girls and the number of individual intakes on which the values at each age are based.

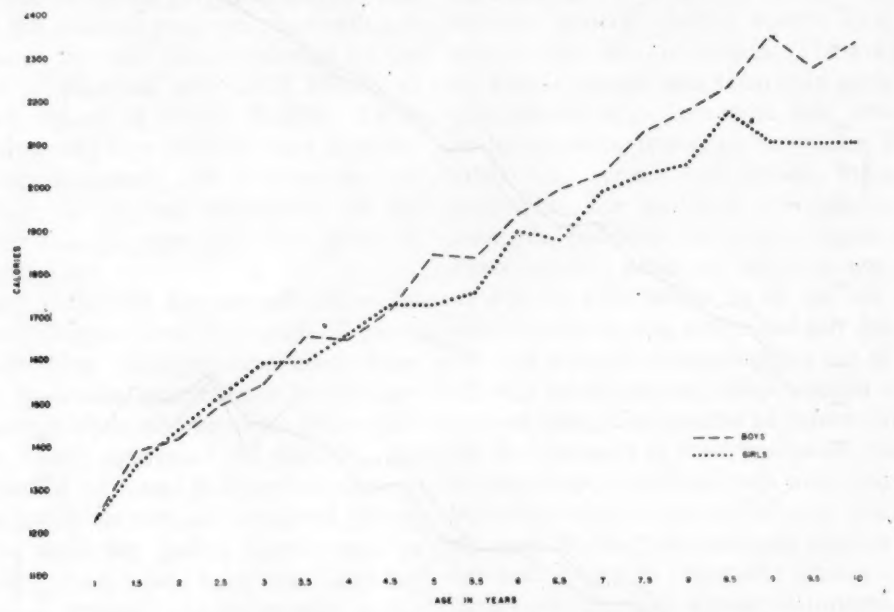

Chart 2.—Average calory consumption by age and sex based on all data from the Harvard School of Public Health growth study.

Calory Consumption by Age, Based on All Data
Harvard School of Public Health Growth Study

Age, Years	Boys				Girls			
	Number	Number of Intakes	Calories		Number	Number of Intakes	Calories	
			Mean	Standard Deviation, Range			Mean	Standard Deviation, Range
1	75	172	1,224	1,017-1,431	80	166	1,224	996-1,452
1½	76	171	1,389	1,151-1,627	82	164	1,356	1,123-1,589
2	90	193	1,418	1,154-1,682	102	189	1,469	1,159-1,719
2½	102	201	1,495	1,221-1,769	100	205	1,516	1,192-1,840
3	113	233	1,542	1,255-1,829	111	198	1,591	1,294-1,888
3½	105	233	1,653	1,361-1,945	111	190	1,594	1,276-1,912
4	99	191	1,645	1,317-1,973	108	206	1,659	1,334-1,984
4½	101	208	1,712	1,407-2,017	107	198	1,725	1,380-2,070
5	105	209	1,842	1,508-2,176	108	224	1,824	1,508-2,080
5½	88	175	1,835	1,491-2,179	92	161	1,753	1,409-2,097
6	96	179	1,932	1,590-2,274	94	146	1,897	1,526-2,268
6½	77	160	1,992	1,611-2,373	71	116	1,875	1,533-2,217
7	77	184	2,026	1,653-2,399	76	143	1,986	1,583-2,389
7½	66	135	2,123	1,713-2,533	63	112	2,025	1,606-2,444
8	72	146	2,170	1,751-2,589	63	110	2,047	1,661-2,433
8½	48	99	2,226	1,729-2,723	46	67	2,168	1,718-2,558
9	58	99	2,345	1,843-2,847	54	88	2,099	1,719-2,479
9½	30	60	2,270	1,830-2,710	26	42	2,093	1,714-2,472
10	42	80	2,328	1,864-2,792	40	63	2,096	1,706-2,486

A comparison is made in chart 3 of our average calory consumption by age, with various standards based on dietary studies and recommended allowances. Only those standards or allowances which have been widely used are included in chart 3.

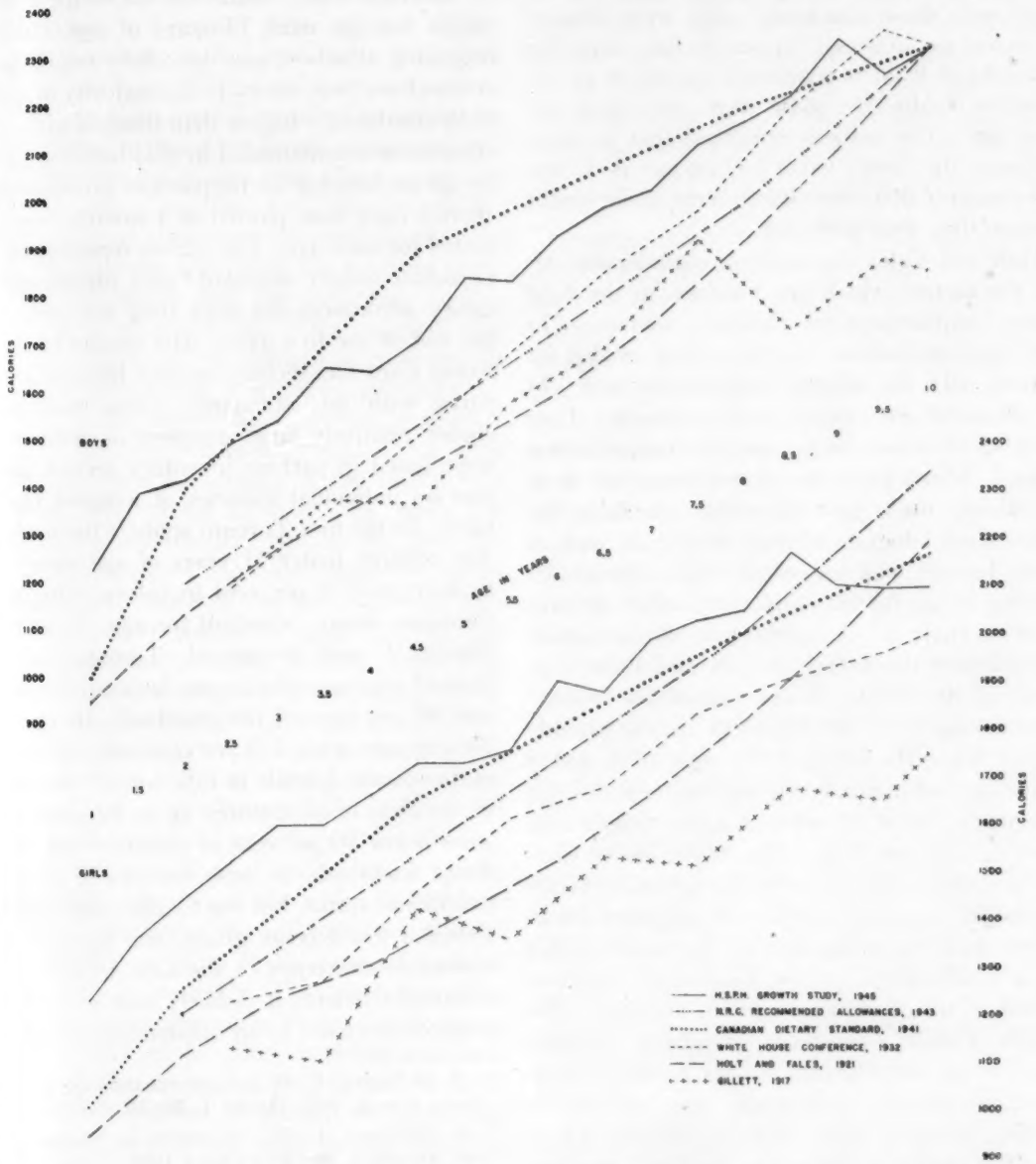

Chart 3.—Average calory consumption by age. A comparison of various standards based on dietary studies recommended allowances.

Gillett [5] reviewed the literature on the subject from 1878 to 1917. This survey, which includes an extensive bibliography, consists of 563 reports, of which 223 were dietary studies, 131 experiments on metabolism and 209 experiments on respiration. The results are given by sex, and values for the first and second years were omitted. Chart 3 shows that the curves representing the average calory intakes of girls and boys as compiled by Gillett are extremely low in comparison with other values. Her values were based mainly on studies of foreign children, mostly German. Holt and Fales [6] called attention to the fact that although these foreign studies have formed the basis of many calculations of calory requirements and have been widely quoted there are

5. Gillett, L. H.: Food Allowances for Healthy Children, Publication 115, New York Association for Improving the Condition of the Poor, 1917.

6. Holt, L. E., and Fales, H. L.: The Food Requirement of Children: I. Total Caloric Requirements, Am. J. Dis. Child. **21**:1-28 (Jan.) 1921.

objections to using them for determining the average calory requirements of healthy American children. They reviewed many of the original reports from the standpoint of the physical well-being of the children studied in comparison with American standards. Many of the children were either overweight or underweight when compared with these standards; some were inmates of orphan asylums and "appear to have been fair examples of what is commonly spoken of as 'institution children'"; some were very small for their age. The authors remarked that in some instances the calory value for the age is so low as to suggest that the children were underweight because they were underfed.

Holt and Fales discussed in considerable detail the factors which are involved in the total energy requirement of children: namely, (1) the basal metabolism, (2) the energy needed for growth, (3) the activity requirement and (4) an allowance for calories lost in excreta. They made no allowance for the specific dynamic action of food. Using their own observations and those of others, they gave theoretic schedules for calories per kilogram of body weight for each of these factors and suggested total calories according to age for boys and girls, which we have used in chart 3. A comparison of the curves representing the values of Holt and Fales with those of the White House Conference report [7] shows values of the latter to be consistently higher for girls between the ages of 4 and 8 years and substantially higher for boys through 9½ years, but at 10 years to agree closely with those of Holt and Fales. The White House Conference standards of calories for age undoubtedly furnished the most widely used suggested allowances until the publication of the recommended dietary allowances of the Food and Nutrition Board of the National Research Council.[8] The White House Conference standards included many of the older foreign studies, to which reference has already been made, later metabolism studies, many of which were on children whose physical condition was not normal, and the various dietary studies of Roberts, whose subjects often included children who were underweight or whose nutritional condition was judged to be fair or poor. In the conclusions of the White House Conference report, attention was called to the inadequacy of the data and to the small number of children on which the average calory intake for age is based.

In the recommended dietary allowances of the Food and Nutrition Board of the National Research Council, which are also shown in chart 3, no differences were made for sex in the average values for age until 13 years of age, although beginning at school age the calory requirements of boys have been shown in the majority of studies to be consistently higher than those of girls. The allowances recommended by this board are given by age periods but for purposes of presentation in chart 3 have been plotted as a smooth curve adjusted for each age. The curves representing the Canadian dietary standard [9] give higher average calory allowances for boys than for girls from the end of the first year. The results of several recent Canadian dietary surveys have been compared with this standard. These surveys included relatively large numbers of children and were based in part on inventory records and in part on individual histories of weighed food intakes. In the first Toronto study,[10] the intakes of 306 children under 11 years of age were found to average 77.5 per cent in calory value of the Canadian dietary standard for age. A survey in Halifax [11] and a second Toronto survey [12] showed averages which were between 94 per cent and 99 per cent of the standard. In Quebec [13] the averages were 110 per cent and 116 per cent of the standard, while in Edmonton [14] 44 per cent of the diets of all children up to 12 years of age were below 90 per cent of the standard. No attempt was made in these surveys to assess the nutritional status, but the families studied represented a low income group, and because of the noticeable deficiency of the diets in some of the essential nutrients it is likely that some of these children were not in an optimal nutritional state.

7. Growth and Development of the Child: III. Nutrition, White House Conference on Child Health and Protection, New York, The Century Company, 1932.

8. Recommended Dietary Allowances, Reprint and Circular Series no. 115, National Research Council, Washington, D. C., 1943.

9. McHenry, E. W.: Determination of Nutritional Status, Canad. Pub. Health J. **32**:231-235 (May) 1941.

10. McHenry, E. W.: Nutrition in Toronto, Canada, Pub. Health J. **30**: 4-13 (Jan.) 1939.

11. Young, E. G.: A Dietary Survey in Halifax, Canad. Pub. Health J. **32**:236-240 (May) 1941.

12. Patterson, J. M., and McHenry, E. W.: A Dietary Investigation in Toronto Families Having Annual Incomes Between $1,500-$2,400, Canad. Pub. Health J. **32**:251-258 (May) 1941.

13. Sylvestre, J. E., and Nadeau, H.: Enquête sur l'alimentation habituelle des familles de petits-salariés dans la ville de Québec, Canad. Pub. Health J. **32**:241-250 (May) 1941.

14. Hunter, G., and Pett, L. B.: A Dietary Survey in Edmonton, Canad. Pub. Health J. **32**:259-265 (May) 1941.

The average caloric values found by Youmans, Patton and Kern [15] in a recent nutritional survey in Tennessee are not shown in chart 3. In studying their data, one is immediately impressed with the fact that from 5 years to 11 years of age the average intake rises only approximately 300 calories. In our series, the same increase occurred between 5 and 8 years of age. When Youman's values are plotted with the other values shown in chart 3, his curve tends to ascend much less rapidly after 5 years of age than the curves of any of the other recent studies. At all these ages his values are well below those obtained in the Canadian and Boston studies. Furthermore, at these ages his mean weights for height and age are well below the expected mean weights for height and age according to the Baldwin and Wood tables. This suggests that the calory intakes of the children at these ages in Youman's survey were frequently inadequate.

Our average calory values shown in chart 3 and the table are consistently higher for girls through 8½ years than any of the values thus far published, except that at 5½ years the Canadian dietary standard reaches the same figure. Our values for boys are somewhat below the Canadian standards between 2½ and 8½ years, but they exceed the latter at 9 years. Our values are somewhat lower for both sexes than those found in a weighed intake study of 21 children between the ages of 8 and 11 years reported by Johnston.[16] She obtained values of 2,490 calories for boys at a mean age of 9 years 4 months and of 2,460 calories for girls at a mean age of 10 years 2 months.

The average and range values given in the accompanying charts and the table are based on all the food intakes of the children from 1 to 10 years of age, a majority of the same children being included at each age. Our average curves presented in the charts, therefore, should reveal the usual changes in calory consumption from year to year during this age period, and the range values should indicate how much variation may be expected at different ages among relatively normal children living in their own homes.

We believe that our values for children over 8½ years of age are too low and that this is due to smaller numbers of children at these ages and to our former lack of appreciation of the need of questioning older children as well as the mothers about the dietary intake. We would expect that at a future date when all the children in our study have passed through these ages these values will require some revision.

Thus far we have made no attempt to sort the cases according to the level of the usual calory intake or to study the various factors related to significant individual differences in intake by age. After such analyses it may be found that age and sex alone are not sufficiently good criteria for the estimation of calory requirements. It may seem advisable to consider size, build or some other characteristic in addition to age and sex.

SUMMARY AND CONCLUSIONS

Average calory values at six month intervals from 1 through 10 years of age are reported for a group of children living at home under normal conditions. The values are based on the dietary intakes of 269 children, of whom 128 are boys and 141 girls. Since a majority of these children were studied at each age, the table of values presented shows the gradual increase with age from 1 to 10 years in calory intake of the same children. This feature of the present study is thought to add appreciably to the significance of the data. The total number of calory intakes on which the values are based is 5,916, of which 3,128 are of boys and 2,788 of girls.

Comparison of the averages, calculated from histories obtained by nutritionists, from intakes recorded by the mothers and from all data, indicates that the best history after 7½ years of age is obtained by questioning both the mother and the child.

Little difference was found between the average calory intake of boys and girls until approximately 5 years of age. At all subsequent ages reported, the values for boys were found to be consistently higher than those for girls. This seems logical when one considers the greater activity of the average boy of school age in comparison with the usual activity of a girl of the same age.

The average calory consumption by age in this study is compared with various standards based on dietary studies and recommended allowances. Present standards or suggested allowances, including those recommended by the Food and Nutrition Board of the National Research Council, have been influenced by the early foreign studies.

It is interesting that as knowledge of food values has been extended and ability to obtain more complete dietary information has increased the calory values have tended to rise. Our values are consistently higher for both boys and girls than those of most earlier reports.

15. Youmans, J. B.; Patton, E. W., and Kern, R.: Surveys of the Nutrition of Populations, Am. J. Pub. Health **33**:58-72 (Jan.) 1943.

16. Johnston, F. A.: Adequacy of a Diet Eaten by Children Eight to Eleven Years of Age, J. Am. Dietet. A. **19**:416-419 (June) 1943.

BASAL METABOLISM OF EIGHT NURSERY SCHOOL CHILDREN DETERMINED AT THREE MONTH INTERVALS

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Data on the basal metabolism of children 2 to 4 years of age are limited. Determination of the normalcy of the basal metabolism of a child is difficult because of the lack of precise values for comparison.

Basal metabolism, as the term is used in this study, means the basic heat production calculated from utilization of oxygen as determined under precise, standard conditions. It does not mean the "irreducible minimum of energy expenditure without which life is impossible."[1] Perhaps "standard metabolism" is a more accurate term, but popular usage prefers the term basal metabolism even when the metabolism is determined according to a certain, specified procedure.

The conditions observed for basal metabolism determinations were as follows: (1) complete muscular relaxation; (2) postabsorptive condition (twelve to fourteen hours after last intake of food); (3) lying awake in a comfortable environment; (4) freedom from physiologic disturbance, as indicated by normal sublingual temperature, normally constant pulse and general healthy appearance, and (5) minimum of mental anxiety and nervous stimulation.

Determination of the basal metabolism of children of this age range, under strict conditions, involves special difficulties because the children do not always understand how to cooperate in the procedure. Lack of cooperation results in failure to obtain consistent and reproducible data. The use of respiration calorimeters and chambers is somewhat less difficult than the use of respiration apparatus, since the former permits the child to be freer from forced restraint and inhibitions. Even though an apparatus which involves the use of a nose clip and mouth piece or a helmet offers complications in maintaining the cooperation of very young subjects, it can be used successfully. Data from older subjects have shown that the two methods of determining basal metabolism give comparable results and can be used interchangeably.[2]

The training of the subject for the procedure is an essential part of a study of this kind. This training must be done in such a way that even a 2 year old child will desire to cooperate in the determination and will feel a sense of accomplishment in having done so successfully. The children derive great satisfaction from the accomplishment of a successful determination. This is reflected in the accuracy of the results obtained.

Workers who are planning a study involving the determination of basal metabolism of children of nursery school age should take care to train their subjects to become accustomed to the apparatus and the procedure.

The difficulties in determining the basal metabolism of children probably have contributed to the wide variations in the data obtained. Some determinations were made on subjects in varying states of physical well-being[3] and others with the child sound asleep.[4] Some subjects had eaten food at various intervals preceding the determination or lacked muscular repose,[4a] whereas for others results were obtained by extrapolation of data on older children. Lewis and his co-workers[5] emphasized the need for carefully controlled conditions in determining the basal metabolism of children.

From the Department of Foods and Nutrition, Texas Technological College.

1. Rose, M. S.: Foundations of Nutrition, New York, The Macmillan Company, 1938, p. 36.

2. Taylor, C. M.: The Energy Metabolism and Mechanical Efficiency of Young Boys, Inaug. Dissert. New York, Columbia University, 1937.

3. (*a*) Wang, C. C.; Kern, R.; Frank, M., and Hays, B. B.: Metabolism of Undernourished Children: Basal Metabolism, Am. J. Dis. Child. **32**:350-359 (Sept.) 1926. (*b*) Mitchell, A. G.; Rittershofer, C. R.; Wang, C. C.; Kaucher, M.; Wing, M., and Hogden, C.: A Metabolic Study of Five Children with the Nephrotic Syndrome, ibid. **55**:27-41 (Jan.) 1938. (*c*) Levine, S. Z., and Wilson, J. R.: The Respiratory Metabolism in Infancy and in Childhood, ibid. **31**:323-334 (March) 1926.

4. (*a*) Benedict, F. G., and Hendry, M. F.: Energy Requirements of Girls from 12 to 17 Years of Age, Boston M. & S. J. **134**:217, 1921. (*b*) Footnote 3.

5. Lewis, R. C.; Kinsman, G. M., and Iliff, A.: The Basal Metabolism of Boys and Girls from 2 to 12 Years Old, Inclusive, Am. J. Dis. Child. **53**:348-420 (Jan., pt. 2) 1937.

Few tables of standards or prediction formulas exist for comparison with actual determinations of basal metabolism of children below 6 years of age. The tables in use usually give levels either far above or below the actual values obtained,[6] and one is uncertain as to what standard to accept in deciding whether an individual determination indicates that the subject is normal.

PURPOSES

The purposes of this study of the basal metabolism of nursery school children were as follows:

1. To determine the basal metabolism of 8 children 2 to 4 years of age, under conditions required by standard basal metabolism procedure.

2. To compare the results with standards existing for children of these ages.

3. To determine the basal metabolism of these subjects at three month intervals for a year in order to observe possible variations.

4. To add to the limited data on the basal metabolism of children 2 to 4 years of age.

SUBJECTS

The subjects were 8 children, 3 girls and 5 boys, selected at random from the applicants for admittance to the Nursery School of the Department of Child Development of the Division of Home Economics, Texas Technological College. The children served as subjects in several other research projects during the year they were in the nursery school. For the basal metabolism determinations, the range in age at the beginning of the tests was from 2 years 4 months to 5 years 9 months. The children were healthy and of normal growth and development, as was shown by pediatric examination. None were excessively overweight or underweight, as appears from table 1. Four subjects were an average of 7.2 per cent overweight, while 4 were an average of 6.3 per cent underweight, with a maximum range of −8.3 to +13.9 per cent for all subjects. Each subject increased in both height and weight during the year.

The subjects were trained for the determination of their basal metabolism by the procedure described by Ling.[7] No determination was attempted until the subject was both willing and able to go through the complete procedure as specified for basal metabolism determinations. At no time was any subject unable to complete the procedure for a determination, and in most cases no difficulty was encountered in obtaining reproducible results.

PROCEDURE

A Collins-Benedict-Roth recording respiration apparatus was used for all determinations, with a rubber-cushioned nose clip and a rubber mouth piece. The nose clip and mouth piece for adults were trimmed to fit the smaller nose and mouth of the child. The children accepted these items readily and were able to breathe through the mouth piece without discomfort, so that in less than a minute records of regular respiration were obtained.

The children were met at their homes as soon as they were awake and in most cases were warmly wrapped and brought to the laboratory in their night clothes. In a few cases the children were dressed in outdoor clothing prior to being carried to an automobile and thence to the laboratory.

On arriving at the laboratory, each child was put comfortably to bed. While he lay quietly in bed, he was closely supervised by an assistant trained for the purpose, who read the child's favorite nursery stories aloud. Sublingual temperature was determined, and two one-half minute pulse counts were made. The pulse was also counted during the determinations of oxygen consumption.

At the end of the twenty to thirty minute rest period, the mouth piece was inserted, the nose clip attached and a recording of the respirations made on graduated kymograph paper, the oxygen consumption being determined according to the accepted procedure for the apparatus. Two determinations of oxygen consumption, each of eight minutes' duration, were recorded each morning, with a few minutes of rest between them. Tests for tightness of the circuit were made during each recording, and at no time was there any indication of a leak. The respiratory tract of the subject formed part of the closed circuit of the apparatus; so both the tightness of the apparatus and its connection to the subject were tested.

At the end of the second determination of oxygen consumption of the subject he was measured and weighed, wearing only shorts. The height and weight were recorded to the closest tenth of an inch and pound respectively, as given in table 1.

Determinations were made on at least two mornings and continued when necessary until the lowest figure obtained for calories per hour agreed within 5 per cent with results obtained on a different morning. This procedure gave a minimum of four recordings for each subject, and in some cases six recordings were made to obtain a "check." The single lowest value was not used to represent the true basal metabolism, since the accuracy of the whole procedure does not warrant its use. Workers[8] have estimated the accuracy of the apparatus and that of the assumption of a respiratory quotient of 0.82 to be within the limits of 5 per cent. One cannot assume the basal metabolism to be the single lowest figure but must assume that it may be any value within 5 per cent of the lowest. Therefore all figures checking within 5 per cent with the lowest were averaged with the lowest to represent the true basal metabolism.

In 28 of the 32 true basal metabolism determinations made on the 8 subjects the results obtained for a subject on the first morning checked with those obtained on the second morning, whereas in 4 true basal metabolism determinations the procedure was repeated on a third morning in order to obtain a "check." In

6. (*a*) Klugh, G. F.: Basal Metabolism in Normal Children from 6 to 12 Years of Age, J. A. M. A. **91**: 202 (July 21) 1928. (*b*) Robb, E.: The Energy Requirement of Normal 3 and 4 Year Old Children Under Standard Basal Metabolism Conditions and During Periods of Quiet Play, Child Development Monograph 16, New York, Teachers College, Columbia University, 1934.

7. Ling, B. C.: The Adaptation of the Preschool Child to Standard Basal Metabolism Conditions, J. Genet. Psychol., to be published.

8. DuBois, E. F.: Basal Metabolism in Health and Disease, ed. 3, Philadelphia, Lea & Febiger, 1936, pp. 121 and 123.

TABLE 1.—*Data on the Basal Metabolism of Subjects*

Subject	Sex	Date *	Age, Yr.-Mo.-Day	Height, Cm.	Weight, Kg.	Deviation from Normal Weight, %	Surface Area, Sq. M.	Calories per Hr.	Metabolism, Calories per 24 Hr. Total	Per Kg.	Per Cm.	Per Sq. M.
1	F	12/17/42	2- 4-12	85.8	12.8	+8.5	0.54	29.6	710	55.5	8.3	1,316
		3/20/43	2- 7-15	87.6	13.6	+3.4	0.56	31.7	761	55.9	8.7	1,358
		7/ 2/43	2-10-27	89.8	14.4	+9.3	0.58	29.7	713	49.5	7.9	1,229
		12/19/43	3- 4-14	92.9	14.7	+4.5	0.60	30.2	725	49.5	7.8	1,208
2	M	12/18/42	3- 4-28	101.3	15.0	−8.3	0.65	34.9	838	55.8	8.3	1,289
		4/ 6/43	3- 8-16	103.6	15.8	−8.0	0.67	38.9	934	59.1	9.0	1,393
		6/22/43	3-11- 1	105.8	15.9	−10.0	0.68	40.9	982	61.8	9.3	1,444
3	M	11/22/42	3- 8- 8	99.7	17.8	+11.2	0.69	39.5	948	53.3	9.5	1,374
		2/20/43	3-11- 7	102.1	18.0	+11.1	0.70	38.8	931	51.7	9.1	1,330
		5/24/43	4- 2-10	103.0	18.6	+7.6	0.72	40.1	962	51.7	9.3	1,336
4	F	12/ 6/42	3- 6-23	100.3	15.0	−8.3	0.64	33.8	811	54.1	8.1	1,267
		3/ 9/43	3- 9-26	102.4	15.7	−2.8	0.66	34.2	821	52.3	8.0	1,244
		5/29/43	4- 0-16	104.6	15.8	−5.9	0.68	36.4	874	55.3	8.4	1,285
		9/23/43	4- 4-10	106.1	16.6	−6.2	0.70	36.3	871	52.5	8.2	1,244
		12/ 8/43	4- 6-25	106.3	17.2	−2.1	0.71	36.8	883	51.1	8.3	1,244
5	F	11/27/42	3- 3-29	94.0	15.0	+6.5	0.61	33.3	799	53.3	8.5	1,310
		2/23/43	3- 6-25	96.1	15.4	+2.9	0.63	34.3	823	53.5	8.6	1,306
		5/29/43	3- 9-26	98.7	16.2	+4.7	0.65	35.5	852	52.6	8.6	1,311
		9/19/43	4- 1-21	101.3	16.7	+1.9	0.68	35.1	842	50.4	8.3	1,239
		12/12/43	4- 4-13	103.3	17.5	+4.1	0.70	37.3	895	51.2	8.7	1,279
6	M	12/23/42	3- 6- 0	99.8	15.1	−5.7	0.64	35.0	840	55.6	8.4	1,313
		3/ 5/43	3- 8-12	102.6	16.0	−2.8	0.67	36.1	866	54.2	8.4	1,293
		6/23/43	4- 0- 0	105.6	16.3	−8.2	0.69	36.4	874	53.6	8.3	1,266
		9/23/43	4- 3- 3	106.3	16.6	−6.4	0.70	36.5	876	52.8	8.2	1,251
		12/15/43	4- 5-22	108.1	17.2	−7.8	0.72	37.7	905	52.6	8.4	1,268
7	M	12/14/42	3- 7-29	106.9	16.7	−2.5	0.70	42.1	1,010	60.5	9.4	1,443
		3/17/43	3-11- 2	109.0	17.4	−7.3	0.73	39.9	958	55.0	8.8	1,312
		6/19/43	4- 2- 4	111.2	17.9	−6.2	0.75	40.7	977	54.6	8.8	1,302
		9/22/43	4- 5- 6	113.0	18.5	−6.8	0.76	41.7	1,001	54.1	8.9	1,317
		12/15/43	4- 8- 0	114.5	18.8	−7.8	0.78	39.9	958	50.9	8.4	1,228
8	M	12/11/42	3- 5- 0	100.8	18.0	+11.1	0.70	38.0	912	50.7	9.1	1,303
		4/ 5/43	3- 7-25	102.3	18.5	+13.9	0.71	39.9	958	51.8	9.4	1,349

* Each date represents an average of two or more days on which basal metabolism determinations were made.

TABLE 2.—*Average Basal Metabolism According to Age Groups*

	Age Group, Yr.	No. of Subjects	Height, Cm.	Weight, Kg.	Surface Area, Sq. M.	Calories per Hr.	Metabolism, Calories per 24 Hr. Total	Per Kg.	Per Cm.	Per Sq. M.
Boys:										
	3-0 to 3-6	2	101.1	16.5	0.68	36.5	875	53.3	8.7	1,296
	3-6 to 4-0	9	103.5	16.8	0.69	39.0	936	55.9	9.0	1,361
							Range:	51.7-61.8	8.4-9.4	1,293-1,444
	4-0 to 4-6	5	107.8	17.6	0.72	39.1	938	53.4	8.7	1,295
							Range:	51.7-54.6	8.2-9.3	1,251-1,336
	4-6 to 5-0	2	113.1	18.0	0.75	38.8	931	52.8	8.4	1,238
Girls:										
	2-0 to 2-6	1	85.8	12.8	0.54	29.6	710	55.5	8.3	1,316
	2-6 to 3-0	2	88.7	14.0	0.57	30.7	737	52.7	8.3	1,294
	3-0 to 3-6	2	93.5	14.9	0.61	31.8	767	51.4	8.2	1,259
	3-6 to 4-0	4	99.4	15.6	0.65	34.5	827	53.1	8.3	1,282
							Range:	52.3-54.1 *	8.0-8.6	1,244-1,311
	4-0 to 4-6	5	104.3	16.8	0.69	36.4	873	52.1	8.4	1,266
							Range:	50.4-55.3	8.2-8.7	1,239-1,285
All subjects:										
	2-0 to 2-6	1	85.8	12.8	0.54	29.6	710	55.5	8.3	1,316
	2-6 to 3-0	2	88.7	14.0	0.57	30.7	737	52.7	8.3	1,294
	3-0 to 3-6	4	97.3	15.7	0.65	34.2	821	52.1	8.5	1,278
	3-6 to 4-0	13*	102.2	16.4	0.68	37.6	902	55.0	8.8	1,327
	4-0 to 4-6	10*	106.1	17.2	0.71	37.8	905	52.8	8.6	1,277

* Weighted average.

of the 28 determinations all 4 recordings, made on o different mornings on each subject, checked within per cent of the lowest value. These results indicate e remarkable relaxation and cooperation achieved these young children and show the reproducibility of e data. Complete confidence is felt that the data tained for these subjects are the true basal metabism figures, representing the minimum oxygen conmption under strictly controlled basal metabolism nditions.

From the calories per hour, the calories per square eter of body surface, the calories per kilogram of dy weight and the calories per centimeter of height ere calculated. These data are recorded in table 1 r each subject for each of the three month intervals, which the true basal metabolism determinations ere made.

For subjects 1, 2, 3 and 8 there are fewer than 5 termination periods, for various reasons, including aving town, difficulty of transportation to the labotory and, in 1 instance, the child's reluctance to return r the fourth determination, though she showed great illingness to come the fifth time.

RESULTS

The calory utilization of the subjects is given table 1. Even though the subjects were fairly omogeneous in size and age, a wide variation ay be expected between the maximum and the inimum calory expenditure when expressed on e basis of units of total size. For all subjects e smallest range in basal metabolism figures is und when metabolism is expressed as calories r square meter of surface area, the maximum alue being about 20 per cent above the minium obtained for any subject. In the range r calories per centimeter and calories per kilogram the maximum values are 23 and 25 per nt above the minimum values respectively.

For individual subjects, the calories per kilogram decrease with increase in age for all except ubjects 2 and 8, on whom only a limited number observations were made. The maximum range etween the highest and the lowest number of alories per kilogram was 9.6 calories, for subject 7; all other subjects showed a range of less han 6 calories.

No consistent variations were observed in alories per centimeter per twenty-four hours, he maximum range being 1 calory per centimeter er twenty-four hours for subjects 3 and 7. On he basis of square meters of surface area, the ariations were of about the same magnitude as hose on the basis of centimeters or kilograms.

Table 2 gives the average basal metabolism of he boys, the girls and all subjects arranged in ge groups of six months each. In a classifiation of this type data for a subject may recur the same, as well as in different, age groups, nce the determination of his metabolism was ade at three month intervals and the divisions according to age were made at six month intervals.

Both boys and girls grew in height and weight during the year. The increases in height and weight were not uniform, the greatest difference being found between the 2 year 6 month to 3 year age group and the 3 year to 3 year 6 month age group.

The average total calories for all subjects increased with increase in age and was proportional to the increases in height and weight of the subjects. When the calories are expressed, on a basis of units of body measurement, no consistent variation occurs with age for these subjects. This fact may be due to the frequency with which the data for a single subject appear in an age group, giving undue emphasis to the data for an individual subject and magnifying any discrepancy they may include.

Table 3 gives the per cent deviation of the basal metabolism of these subjects from the four

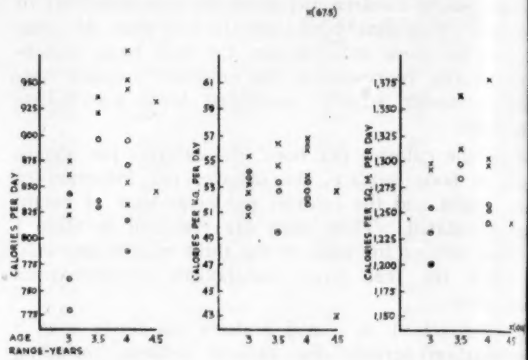
TABLE 3.—*Per Cent Deviation of Basal Metabolism of the Subjects from Standards*

Subject	Sex	Age, Yr.-Mo.-Day	Per Cent Deviation from Standards: Benedict, Height	Dreyer, Height	Talbot, Height	Talbot, Weight
1	F	2- 4-12	+17.0	—16.6	+11.6	+ 9.6
		2- 7-15	+24.5	—11.9	+16.7	+12.9
		2-10-27	+15.7	—19.8	+ 7.1	+ 2.0
		3- 4-14	+15.8	—19.3	+ 5.4	+ 2.2
		Average	+18.3	—16.9	+10.2	+ 6.7
4	F	3- 6-23	+19.6	—10.3	+10.3	+12,9
		3- 9-26	+18.0	—11.2	+ 9.6	+11.2
		4- 0-16	+22.1	— 5.7	+13.5	+17.9
		4- 4-10	+19.2	— 8.4	+12.1	+14.3
		4- 6-26	+20.5	— 6.3	+13.6	+12.8
		Average	+19.9	— 8.4	+11.8	+13.2
5	F	3- 3-29	+26.8	—11.9	+14.9	+11.3
		3- 6-25	+27.6	—10.1	+16.1	+12.7
		3- 9-26	+28.1	— 9.3	+17.0	+13.1
		4- 1-21	+22.6	—11.7	+13.5	+ 9.8
		4- 4-13	+27.3	— 8.3	+18.4	+13.4
		Average	+26.5	—10.3	+16.0	+12.1
		Benedict-Talbot				
2	M	3- 4-28	+15.6	—19.6	+ 5.9	+15.6
		3- 8-16	+24.7	— 8.8	+16.6	+25.4
		3-11- 1	+30.6	— 4.5	+21.2	+31.3
		Average	+23.6	—11.0	+14.6	+24.1
3	M	3- 8- 8	+18.5	—12.7	+20.8	+17.9
		3-11- 7	+15.7	—14.8	+17.4	+15.0
		4- 2-10	+17.3	—13.4	+20.7	+16.2
		Average	+17.2	—13.6	+19.6	+16.4
6	M	3- 6- 0	+15.4	—16.1	+ 7.0	+15.4
		3- 8-12	+14.7	—14.0	+ 8.7	+15.5
		4- 0- 0	+14.5	—16.0	+ 8.2	+15.2
		4- 3- 3	+13.8	—16.6	+ 8.1	+14.1
		4- 5-22	+15.3	—15.3	+10.4	+15.1
		Average	+14.7	—15.6	+ 8.5	+15.1
7	M	3- 7-29	+30.7	— 4.1	+23.9	+31.0
		3-11- 3	+21.3	—10.9	+16.1	+21.0
		4- 2- 4	+21.6	—10.4	+16.4	+21.1
		4- 5- 6	+22.3	— 9.4	+16.8	+21.3
		4- 8- 0	+16.1	—12.1	+ 9.5	+14.9
		Average	+22.4	— 9.4	+16.5	+21.9
8	M	3- 5- 0	+13.3	—20.1	+15.6	+12.6
		3- 7-25	+17.1	—13.6	+20.8	+16.1
		Average	+15.2	—16.9	+18.2	+14.4
Weighted average						
Benedict, height			+21.8			
Benedict-Talbot			+18.8	—12.3	+13.9	+15.3

standards recommended for children.[9] These data illustrate the need for more accurate standards for children. The extremes found ranged from + 31 per cent, for subject 7, for the Talbot weight standard, to — 20.1 per cent, for subject 8, for the Dreyer standard. The greatest difference lies between the Benedict height and the Dreyer standard. In fact, Dreyer's is the only formula for a standard giving a consistently negative deviation.

The work reported in the literature on the basal metabolism of children is so limited that results are difficult to compare. This is especially true of work with children younger than 5 years. The results are further complicated by lack of uniformity in the procedures employed and in the purposes for which the study was being done. Many subjects were studied to observe their physiologic changes rather than to determine the metabolism of the healthy, normal child.

The basal metabolism per unit of body measurement is comparable for the subjects of the two studies and shows no significant variations.



Basal metabolism of children of four age groups, as reported by various workers. The small crosses indicate values for boys; the small circles, values for girls.

TABLE 4.—*Data on Subjects of Comparable Age Groups from Other Studies*

Worker	No. of Subjects	Age, Yr.-Mo.	Sex	Height, Cm.	Weight, Kg.	Surface Area, Sq. M.	Calory Expenditure per Day			
							Total	Per Kg.	Per Cm.	Per Sq. M.
Robb [6b]	6	3-0 to 3-6	F	100.5	15.6	0.65	841	54.4	8.4	1,292
	7	3-6 to 4-0	F	102.3	17.1	0.69	898	52.9	8.8	1,299
	4	4-0 to 4-5	F	106.8	17.2	0.72	892	51.8	8.4	1,239
	5	3-0 to 3-6	M	98.3	15.7	0.64	831	52.9	8.5	1,289
	3	3-6 to 4-0	M	103.5	16.9	0.70	920	54.6	8.9	1,310
	4	4-0 to 4-5	M	103.2	16.8	0.69	950	56.9	9.2	1,379
Mitchell [3b]	1	2-11	M	92.5	16.2	0.69	823	50.7	8.8	1,200
	1	3-1	F	85.8	13.6	0.61	729	53.8	8.5	1,200
	1	4-6	M	107.0	19.7	0.79	847	43.2	7.9	1,068
Williams [11b]	1	3-0 to 3-6	M	98.6	15.5	....	861	55.5*	8.7*	.....
	2	3-6 to 4-0	F	98.6	16.8	....	833	49.6*	8.4*	.....
	1	4-0 to 4-6	M	103.9	17.3	....	979	56.6*	9.4*	.....
Wang [3a]	1	4	M	103	12.6	....	851	67.5	8.3*	.....
	3	4	F	103	15.4	....	815	53.3	7.9*	.....
Nakagawa [11c]	5	4	M	99.4	15.0	0.64	835	55.8	8.4*	1,306*
	1	4	F	98.1	15.0	0.63	789	52.6	8.1*	1,252*

* Values calculated from data given.

Table 4 gives a comparison of the results of some of the studies reporting on the same age groups. The results obtained by Robb [10] best parallel those of the present investigation. A comparison of the results of the two studies can be made from tables 2 and 4. The girls of Robb's study were taller and heavier, but the boys were slightly shorter, than the corresponding subjects of this study. The smaller average stature of the girls in the present study can be attributed mostly to subjects 1 and 5, who were both stockily built.

Neither do the data of other workers [11] show significant differences. When all values for each age group are plotted, they show great homogeneity, as illustrated in the accompanying chart. The values presented are not entirely comparable because the studies did not include the same number of subjects nor were the determinations made on the subjects in exactly comparable conditions. Except in 2 instances the metabolism varied less when expressed as calories per kilogram than when expressed as calories per square meter or as total calories.

9. (*a*) Carpenter, T. M.: Tables, Factors and Formulas for Computing Respiratory Exchange and Biological Transformations of Energy, ed. 2, Washington, D. C., Carnegie Institution of Washington, 1924. (*b*) Talbot, F. B.: Basal Metabolism Standards for Children, Am. J. Dis. Child. **55**:455-459 (March) 1938.

10. Robb,[6b] p. 11.

11. (*a*) Mitchell and others, [3b] p. 36. (*b*) Williams, D. M.: Influence of Sleep on the Energy Metabolism of Three and Four-Year-Old Children, Inaug. Dissert., New York, Columbia University, 1934. (*c*) Wang and others,[3a] p. 352. (*b*) Wang, C. C., and Kern, R.: The Influence of Sleep on Basal Metabolism of Children, Am. J. Dis. Child. **36**:83-88 (July) 1928. (*d*) Nakagawa, I.: Growth and Basal Metabolism: I. Basal Metabolism of Preschool Children, Am. J. Dis. Child. **47**:963-969 (May) 1934.

All authors reported a negative deviation of their results from the formula of Dreyer and positive deviations from the standards developed by Benedict and Talbot. Dreyer's formula was not planned for children less than 5 years old and has been found not to give good results for children older than 5 years, even though it is quite accurate in predicting the metabolism of adults. The great discrepancy between actual results and available standards is obvious, and is evidence that more work must be done on the basal metabolism of children.

Talbot [12] expressed the belief that metabolism of children is not represented by a simple plus or minus deviation from a standard but involves several factors, including geographic location and different rates of maturation, not indicated by chronologic age. He found that the day by day metabolism of children varied more than that of adults.

Nakagawa [13] interpreted his data to indicate that the metabolism of children varies with the season; he found the maximum expenditure of energy to be in January and the minimum in July. MacLeod and Rose [14] presented data which showed no difference as to the season when the metabolism was determined. Some children showed differences between their metabolism in winter and that in summer, but these differences were not consistent; other children showed no such differences.

The implications of these data are that probably various stages of maturation exist in children of the same chronologic age. Furthermore, basal metabolism is related to the rate and extent of maturation. For this reason basal metabolism values for children cannot be compared successfully on the basis of chronologic age; the basis must allow for the developmental progress of the child. It is necessary that standards make these allowances in order to predict accurately the basal metabolism of a child. Furthermore, workers need to agree on the procedure to be accepted and used to determine the basal metabolism of children.

12. Talbot, [9b] p. 458.

13. Nakagawa, I.: Growth and Basal Metabolism: V. Changes in Basal Metabolism of Children During Year, Am. J. Dis. Child. **49**:1232-1239 (May) 1935.

14. MacLeod, G., and Rose, M. S.: Some Factors Influencing the Basal Metabolism of Children, J. Biol. Chem. **67**:xix-xx, 1926.

Case Reports

PYOPNEUMOTHORAX IN A PREMATURE BABY SUCCESSFULLY TREATED WITH PENICILLIN

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Prior to the use of penicillin in the treatment of staphylococcic infection, empyema caused by the staphylococcus resulted in a mortality in children of approximately 34 per cent. Ladd and Swan [1] recently reviewed the mortality statistics in 33 cases of staphylococcic empyema in infants and children. These patients were treated by various methods. Of the 33 patients, 29 were under 1 year of age, and 12 of these were under 4 months of age. The fatality rate in the latter group was 66 per cent. The fatality rate in the remaining group, of 21, was 4.3 per cent. More recently Riley [2] analyzed 29 cases at Babies Hospital in New York and found that 76 per cent of the patients were in the first year of life and the majority of them were under 3 months of age. The mortality rate was 34.5 per cent, but patients of all ages were included.

McBryde [3] has recently reported 2 cases of pneumonia due to the hemolytic staphylococcus in young infants which was successfully treated with penicillin. He stated that there had hitherto been no published reports on the use of penicillin in the treatment of pneumonia due to hemolytic Staphylococcus aureus in young infants.

Leach and Holland [4] reported the case of a premature baby with pulmonary abscesses due to the staphylococcus, who recovered after administration of sulfathiazole and repeated aspiration.

The report of the following case seems justified because of the age and immaturity of the patient, the low total amount of penicillin employed and the lack of response to sulfonamide therapy.

REPORT OF A CASE

J. K. was born Dec. 10, 1943, four weeks prematurely, by cesarean section, performed by Dr. O. Robbins. The baby weighed 5 pounds ½ ounce (2,28 Gm.). Shortly after birth the baby began to have cyanotic spells, necessitating continuous administration of oxygen. He was subjected to laryngoscopic examination, and a small amount of amniotic fluid and mucus was aspirated by Dr. L. Boies. Roentgenographic examination at this time revealed partial atelectasis of the upper portion of the right lung (fig. 1). After aspiration, the infant's condition rapidly improved and remained good. The roentgenogram of the chest became clear. Administration of oxygen was discontinued, and the child was given the care routinely provided for premature babies in an incubator.

On December 30, twenty days after the baby's birth, his temperature rose to 101 F. The following day it rose to 102.4 F. Respirations were rapid, the color

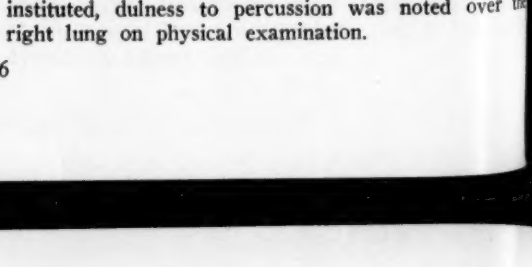

Fig. 1.—*A*, atelectasis of the upper lobe of the right lung; *B*, pyopneumothorax in an infant 1 month old.

poor and the abdomen greatly distended. A roentgenogram of the chest revealed pneumothorax, with atelectatic areas throughout the right lung. The leukocyte count was 26,000 per cubic millimeter, 81 per cent of which were polymorphonuclears. Suction was instituted, and administration of oxygen was resumed. An initial dose of 0.2 Gm. of sulfamerazine per pound (453 Gm.) of body weight followed by 0.2 Gm. of sulfamerazine per pound daily was given. In spite of this treatment, the course of the illness was obviously unfavorable; the dyspnea and cyanosis became more pronounced, and the temperature remained at about 102 F. The sulfamerazine level in the blood on January 4 was 6 mg. per hundred cubic centimeters, and the dose was increased to 0.5 Gm. per pound of body weight every twenty-four hours. This procedure was not followed by any improvement. On January 7, seven days after treatment had been instituted, dulness to percussion was noted over the right lung on physical examination.

Read before the Northwestern Pediatric Society, Nov. 10, 1944, at Bayport, Minn.

1. Ladd, W. E., and Swan, H.: Mortality in Acute Staphylococcal Empyema in Infants and Children, J. Pediat. **23**:297-302 (Sept.) 1943.

2. Riley, C. M.: Staphylococcus Empyema in Infants and Children, J. Pediat. **24**:577-584 (May) 1944.

3. McBryde, A.: Hemolytic Staphylococcus Pneumonia in Early Infancy: Response to Penicillin Therapy, Am. J. Dis. Child. **68**:271-272 (Oct.) 1944.

4. Leach, W., and Holland, M.: Abscesses of the Lung in a Premature Baby, Am. J. Dis. Child. **68**: 324-326 (Nov.) 1944.

Roentgenograms revealed fluid in the right pleural cavity, with displacement of the heart and the mediastinum toward the left. On aspiration 24 cc. of thick purulent material was withdrawn from the pleural cavity. Hemolytic Staph. aureus (coagulase positive) was obtained in pure culture from the fluid.

The following day, January 8, administration of sulfamerazine was discontinued, the level in the blood having reached 10 mg. per hundred cubic centimeters. Administration of penicillin was started; 3,000 Oxford units was given intravenously, and 3,000 units was instilled into the pleural cavity, after removal of 60 cc. of thick purulent material, and 666 units was given every three hours intramuscularly. The infant breathed more easily and was more comfortable after the aspiration. On January 9 30 cc. of the fluid, which was much thinner, was removed by aspiration from the pleural cavity, and again 3,000 units of penicillin was injected into this space. Pour plates of the aspirated material, obtained on January 8 and 9, are shown in figure 2. Clinically, the child was much improved, and his temperature reached normal. The respiration became lower and less labored. On January 10 a roentgenogram showed only a small amount of fluid, encapsulated in the upper lobe of the right lung; the heart and the mediastinum had returned essentially to a normal position. Aspiration of the pleural cavity on January 11 yielded only 2 cc. of straw-colored fluid. The bacterial count on the first aspiration was 73,000 organisms per cubic centimeter of fluid. A progressive and pronounced decrease in the bacterial count was noted on each aspiration. The clinical course continued to show improvement, although the infant was still receiving oxygen continuously. A final aspiration of the pleural cavity, done on January 15, yielded only a few drops of light fluid. A roentgenogram revealed a biloculated air pocket in the posthilar region, which in subsequent films was shown to have been completely absorbed. The use of oxygen was gradually discontinued over a period of three days. The use of penicillin was discontinued on January 23, fifteen days after it had been started.

The baby's nutrition remained good throughout the treatment, and at no time did he have a major gastrointestinal disturbance. Cultures of blood taken January 8, before penicillin was administered, were sterile. The leukocyte count gradually returned to normal. Roentgenograms taken before the infant's discharge revealed a slightly thickened pleura in the right axillary region. The lung was normally ventilated, and the air pocket in the posterior part of the right hilus was very small. Supportive measures in the treatment consisted of three intravenous transfusions of citrated blood (total 90 cc.) and parenteral administration of fluids. The infant was given breast milk when this was available; at other times a simple evaporated milk formula was used, with the addition of preparations of vitamin C, A and D. His weight on his discharge was 8 pounds 4 ounces (3,750 Gm.).

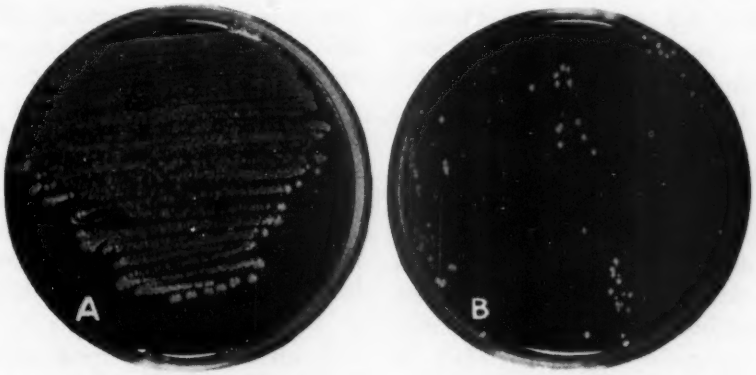

Fig. 2.—Pour plates showing growth of hemolytic staphylococci before and after use of penicillin.

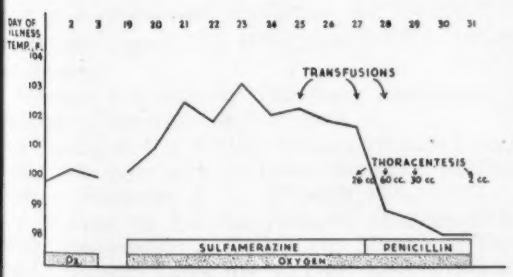

Fig. 3.—Clinical chart of infant with pyopneumothorax.

COMMENT

Administration of penicillin was started seven days after the onset of pyopneumothorax in a premature infant. It appeared that sulfamerazine was failing to influence the course of the disease. Penicillin was given over a period of fifteen days.

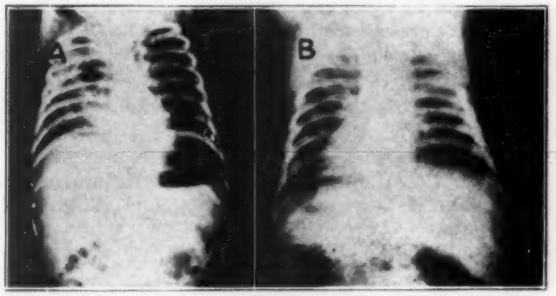

Fig. 4.—*A*, disappearance of fluid after aspiration and administration of penicillin; *B*, normal chest five weeks after onset of pyopneumothorax.

A total of approximately 40,000 Oxford units was given, 9,000 units was given intrapleurally, 3,000 units intravenously and a total of 27,000 units intramuscularly. Repeated urinalysis throughout the illness revealed nothing abnormal. The hemoglobin content ranged from 9 to 12 Gm. per hundred cubic centimeters.

SUMMARY

The possibility and early recognition of pulmonary infection following atelectasis in the premature infants should be emphasized. Direct laryngeal suction is of value in treating th condition.

Whereas patients yielding pneumococci an streptococci on aspiration usually respond t prompt and adequate sulfonamide therapy, pa tients whose condition is due to staphylococci pathogens apparently require the antibiotic ac tivity of penicillin. It would seem that a rela tively small total dose (40,000 units) of penicilli suffices even for severe infection in the prematur baby.

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Progress in Pediatrics

HISTOPLASMOSIS IN CHILDREN

REVIEW OF THE LITERATURE, WITH REPORT OF A CASE

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In January 1906, Strong [1] described an ulcerative cutaneous lesion which simulated the Delhi boil. His patient was a Filipino woman 35 years of age. Biopsy revealed that the tissues surrounding the lesion contained macrophages which were filled with parasites, resembled "cockle shells" and measured 3 to 4 microns in diameter. He expressed the opinion that the parasites belonged to the Blastomyces group of organisms and that they had not been described previously.

Although this has been stated to be the first case of histoplasmosis reported in the literature,[2] Strong himself stated (in a personal communication to Parsons) that he was of the opinion that this case was an instance of infection in man by Cryptococcus farciminosus. In April 1906, Darling [3] reported from the Canal Zone his first case of what he called "a protozoan infection producing pseudotubercles in the lungs and focal necrosis in the liver, spleen and lymph nodes." He suggested the name "Histoplasma capsulatum" for the organism and "histoplasmosis" for the disease. He regarded the organisms as a protozoan, similar to the members of genus Leishmania. In 1908 [4] and 1909 [5] Darling reported 2 more cases of a similar infection encountered in the Canal Zone.

In 1912, Rocha-Lima [6] studied Darling's organism and noted its resemblance to C. farciminosus, the fungus of epizootic lymphangitis in horses. This was the first time that the organism was considered to be a fungus. In 1924, Riehl [7] reported from Vienna a case of generalized fungus infection of seven years' duration. The photomicrographs of the involved organs, however, showed typical Histoplasma capsulatum. In 1926, Riley and Watson [8] from Minnesota and Phelps and Mallory [8] from Honduras reported cases of histoplasmosis, and after these publications reports began appearing from all over the world, but particularly from the United States.

In 1934, DeMonbreun [9] cultivated the organism for the first time from a patient studied by Dodd and Tompkins.[10] From this culture, De Monbreun was able to establish definitely that

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1. Strong, R. P.: A Study of Some Tropical Ulcerations of the Skin with Particular Reference to Their Etiology, Philippine J. Sc. **1**:91-115, 1906.

2. Meleney, H. E.: Histoplasmosis (Reticulo-Endothelial Cytomycosis): A Review with Mention of Thirteen Unpublished Cases, Am. J. Trop. Med. **20**:603-616 (July) 1940.

3. Darling, S. T.: A Protozoön General Infection Producing Pseudotubercles in the Lungs and Focal Necroses in the Liver, Spleen and Lymph Nodes, J. A. M. A. **46**:1283-1285 (April. 28) 1906.

4. Darling, S. T.: Histoplasmosis: A Fatal Infectious Disease Resembling Kala-Azar Found Among Natives of Tropical America, Arch. Int. Med. **2**:107-123 (Sept.) 1908.

5. Darling, S. T.: The Morphology of the Parasite (Histoplasma Capsulatum) and the Lesions of Histoplasmosis, a Fatal Disease of Tropical America, J. Exper. Med. **11**:515-531 (July) 1909.

6. Cited by Meleney.[2]

7. Riehl, G., Jr., cited by Moore, M., and Jorstad, L. H.: Histoplasmosis and Its Importance to Otorhinolaryngologists: A Review with Report of a New Case, Ann. Otol., Rhin. & Laryng. **52**:779-815 (Dec.) 1943.

8. Riley, W. A., and Watson, C. J.: Histoplasmosis of Darling, with Report of a Case Originating in Minnesota, Am. J. Trop. Med. **6**:271-282 (July) 1926.

9. DeMonbreum, W. A.: The Cultivation and Cultural Characteristics of Darling's Histoplasma Capsulatum, Am. J. Trop. Med. **14**:93-125 (March) 1934.

10. Dodd, K., and Tompkins, E. H.: A Case of Histoplasmosis of Darling in an Infant, Am. J. Trop. Med. **14**:127-137 (March) 1934.

the organism was a fungus and to classify it as "Coccidioideaceae and of the genus Posadasia." In 1940, Meleney [2] reviewed the literature and mentioned 13 additional previously unreported cases. Since then, with the case that we are reporting, approximately 50 more cases have been reported, which makes a total of 81 cases at the present time.[11] Since in 21 of these cases the disease occurred in children, of whom 15 we infants less than 15 months of age, a summary the features of the disease as it affects childr may be of value.

REPORT OF CASE

CASE 1.—The patient, a girl, was born Oct. 12, 19 after seven months of gestation. The infant weigh 3 pounds 8 ounces (1,533 Gm.) at birth, gained w on breast milk and artificial feeding and was dismiss from the hospital and admitted to the Catholic Infa Home in St. Paul on December 1. At that time s weighed 6 pounds (2,722 Gm.). The infant's moth was living and well and had one other child, aged years, who was also well. The health of the father the patient was not known.

Physical examination on the infant's entrance to t Home gave negative results. On December 4, at t age of 54 days, the infant had frequent loose stool Since several children in the institution had had diarrh at that time, it was felt that the infant had contract enteritis. Physical examination revealed nothing signi cant. She continued to have intermittent foul-smelli diarrheal stools, however, and failed to gain weigh On December 27, pronounced abdominal distention a slight icterus were noted and the liver and spleen we palpable.

11. (*a*) Agress, H., and Gray, S. H.: Histoplasmosis and Reticuloendothelial Hyperplasia, Am. J. Dis. Child. **57**:573-589 (March) 1939. (*b*) Amolsch, A. L., and Wax, J. H.: Histoplasmosis in Infancy: Report of a Case, Am. J. Path. **15**:477-482 (July) 1939. (*c*) Anderson, W. A. D.; Michelson, I. D., and Dunn, T. M.: Histoplasmosis in Infancy: Report of a Case, Am. J. Clin. Path. **11**:344-355 (April) 1941. (*d*) Beamer, P. R.; Smith, E. B., and Barnett, H. L.: Histoplasmosis: Report of a Case in an Infant and Experimental Observations, J. Pediat. **24**:270-280 (March) 1944. (*e*) Boltjes, B.: Histoplasmosis: Report of a Case with Brief Review of the Literature, J. Kansas M. Soc. **44**:226-229 and 234 (July) 1943. (*f*) Broders, A. C.; Dochat, G. R.; Herrell, W. E., and Vaughn, L. D.: Histoplasmosis Producing Vegetative Endocarditis: Review of Literature, with Report of a Case, J. A. M. A. **122**:489-492 (June 19) 1943. (*g*) Brown, A. E.; Havens, F. Z., and Magath, T. B.: Histoplasmosis: Report of a Case, Proc. Staff Meet., Mayo Clin. **15**:812-816 (Dec. 18) 1940. (*h*) Buie, R. M., Jr.: Histoplasmosis of Darling: First Reported Case in North Carolina, J. Bowman Gray School Med. **1**:112-116 (Sept.) 1943. (*i*) Clemens, H. H., and Barnes, M. L.: Histoplasmosis of Darling: Report of a Case, South. M. J. **33**:11-15 (Jan.) 1940. (*j*) Colvin, S. H., Jr.; Gore, I., and Peters, M.: A Case of Histoplasmosis (Darling) with Autopsy, Am. J. M. Sc. **207**:378-385 (March) 1944. (*k*) Crumrine, R. M., and Kessel, J. F.: Histoplasmosis (Darling) Without Splenomegaly, Am. J. Trop. Med. **11**:435-449 (Nov.) 1931. (*l*) Dean, L. W., Jr.: Histoplasmosis of the Larynx, Arch. Otolaryng. **36**:390-392 (Sept.) 1942. (*m*) Derry, D. C. L.; Card, W. I.; Wilson, R., and Duncan, J. T.: Histoplasmosis of Darling: Report of a Case; Mycological Note, Lancet **1**:224-227 (Feb. 21) 1942. (*n*) German, W. M.; Ashmun, S., and Dille, C. E.: Histoplasmosis: Case Report, Am. J. Clin. Path. **13**:12-14 (Jan.) 1943. (*o*) Gunter, W. A., and Lafferty, C. R.: Histoplasmosis of Darling: Report of a Case, J. M. A. Alabama **9**:337-339 (April) 1940. (*p*) Hansmann, G. H., and Schenken, J. R.: A Unique Infection in Man Caused by a New Yeast-Like Organism, a Pathogenic Member of the Genus Sepedonium, Am. J. Path. **10**:731-738 (Nov.) 1934. (*q*) Henderson, R. G.; Pinkerton, H., and Moore, L. T.: Histoplasma Capsulatum as a Cause of Chronic Ulcerative Enteritis, J. A. M. A. **118**:885-889 (March 14) 1942. (*r*) Hild, J. R.: Histoplasmosis in Infancy, Am. J. Dis. Child. **63**:131-139 (Jan.) 1942. (*s*) Humphrey, A. A.: Reticuloendothelial Cytomycosis (Histoplasmosis of Darling), Arch. Int. Med. **65**:902-918 (May) 1940. (*t*) Key, J. A., and Large, A. M.: Histoplasmosis of the Knee, J. Bone & Joint Surg. **24**:281-290 (April) 1942. (*u*) Palmer, A. E.; Amolsch, A. L., and Shaffer, L. W.: Histoplasmosis with Mucocutaneous Manifestations: Report of a Case, Arch. Dermat. & Syph. **45**:912-916 (May) 1942. (*v*) Ramsey, T. L., and Applebaum, A. A.: Histoplasmosis "Darling," Am. J. Clin. Path. **12**:85-94 (Feb.) 1942. (*w*) Reid, J. D.; Scherer, J. H Herbut, P. A., and Irving, H.: Systemic Histopla mosis: Systemic Histoplasmosis Diagnosed Befo Death and Produced Experimentally in Guinea Pig J. Lab. & Clin. Med. **27**:419-434 (Jan.) 1942. (*x*) Rhodes, P. H.; Conant, N. F., and Glesne, L. R. H Histoplasmosis: Report of Case in an Infant 3 Month of Age, J. Pediat. **18**:235-241 (Feb.) 1941. (*y*) Shaffe F. J.; Shaul, J. F., and Mitchell, R. H.: Histopla mosis of Darling: Fourth Case to Be Reported United States, J. A. M. A. **113**:484-488 (Aug. 5) 19 (*z*) Schlumberger, H. G., and Service, A. C.: A Ca of Histoplasmosis in an Infant with Autopsy, Am. M. Sc. **207**:230-239 (Feb.) 1944. (*a'*) Scott, E. P Histoplasmosis: Report of a Case in an Infant Months of Age, J. Pediat. **19**:668-671 (Nov.) 19 (*b'*) Simpson, F. W., and Barnetson, J.: Histopla mosis: Report of Case, J. Path. & Bact. **54**:299-3 (July) 1942. (*c'*) Thomas, W. C., and Morehea R. P.: Histoplasmosis: Report of a Case in Nor Carolina, North Carolina M. J. **4**:378-382 (Sept.) 19 (*d'*) Van Pernis, P. A.; Benson, M. E., and Holinge P. H.: Specific Cutaneous Reactions with Histopla mosis: Preliminary Report of Another Case, J. M. A. **117**:436-437 (Aug. 9) 1941. (*e'*) William R. H., and Cromartie, W. J.: Histoplasmosis: Repo of a Case, Ann. Int. Med. **13**:2166-2171 (May) 19 (*f'*) Wood, W. B., Jr., and Moore, R. A.: Case R ports of Barnes Hospital: Clinical and Postmort Records Used in Weekly Clinicopathologic Conferenc at Barnes Hospital, St. Louis, J. Missouri M. A. 4 251-259 (Aug.) 1943. (*g'*) Wright, R. B., and Hacht F. W.: Histoplasmosis of Darling: Report of a Ca Ann. Int. Med. **15**:309-319 (Aug.) 1941. (*h'*) Pa sons, R. J., and Zarafonetis, C. J. D.: Histoplasmos in Man: Report of Seven Cases and a Review Seventy-One Cases, Arch. Int. Med. **75**:1-23 (Jan 1945. (*i'*) Strong.[1] (*j'*) Meleney.[2] (*k'*) Darling (*l'*) Darling.[4] (*m'*) Darling.[5] (*n'*) Riehl.[7] (*o'*) Rile and Watson.[8] (*p'*) DeMonbreun.[9] (*q'*) Dodd a Tompkins.[10]

The patient's course continued downhill, and on Jan. 13, 1944 she was transferred to St. Joseph's Hospital, St. Paul. On admission to the hospital the patient weighed 6 pounds 14 ounces (3,118 Gm.). Thus, she gained 14 ounces (396 Gm.) in six weeks. The outstanding physical observations were rectal temperature of 101 F., pronounced distention of the abdomen and a slightly enlarged liver and spleen. There was a slight icteric tinge to the scleras and skin.

The Wassermann test of the blood, examination of the urine, an excretory urogram, roentgenographic studies of the chest and roentgenologic examination of the colon after a barium sulfate enema gave negative results. Cultures of the stools were negative for organisms of the typhoid and dysentery groups. The Mantoux test gave negative results with old tuberculin in dilutions of 1 : 1,000 and 1 : 100. No definite diagnosis was reached at this time.

The child was given various feedings and repeated transfusions of whole blood and plasma, and by January 23 she seemed somewhat improved. The abdominal distention and the intermittent loose foul-smelling stools continued, but she had gained approximately 1 pound (453 Gm.). The rectal temperature varied from 100 to 102 F. Hematologic studies on January 23 revealed a hemoglobin content of 94 per cent and 4,700,000 erythrocytes per cubic millimeter of blood.

The infant's condition failed to improve in the ensuing weeks, and on February 8 icterus had become more pronounced and the previous symptoms continued. The van den Bergh reaction was immediate and direct. The concentration of serum bilirubin was 3.2 mg. per hundred cubic centimeters and of blood cholesterol 120 mg. A tentative diagnosis of malignant lesion was made at this time.

On February 28, a peculiar pustular rash appeared on the chest and back, for which a diagnosis of pyoderma was made. The liver and spleen were enlarged more noticeably, icterus had increased in intensity and the patient's condition seemed definitely worse. Studies of the blood revealed a concentration of hemoglobin of 50 per cent, 2,560,000 erythrocytes and 5,550 leukocytes, of which 59 per cent were polymorphonuclear leukocytes, 30 per cent lymphocytes and 11 per cent monocytes. Definite achromasia, anisocytosis and poikilocytosis were observed. A diagnosis of severe secondary anemia of unknown origin was made. The patient's course continued downhill; the rectal temperature ranged from 103 to 104 F. and terminally she showed signs of diffuse bronchopneumonia. She died on March 16, at the age of 5 months, approximately fifteen weeks after the onset of her symptoms.

Necropsy.—Necropsy was performed by one of us (Tenen). The body was that of a well developed, severely emaciated white infant, weighing 3,175 Gm. and measuring 57 cm. from crown to heel. Pronounced cyanosis and moderate hypostasis and rigor were noted. Edema and jaundice were not observed. The liver and spleen could be palpated through the distended abdominal wall.

When the peritoneal cavity was opened, the peritoneal surfaces were smooth, glistening and transparent, and there was no excess fluid. The liver and spleen were enlarged. The dome of the diaphragm arched to its normal attachments; the umbilical veins and artery were occluded and showed no abnormalities. The normal relationship of organs was maintained, and no congenital abnormalities were noted. The appendix lay in the right lower quadrant and showed nothing significant.

When the thorax was opened, the pleural surfaces were smooth and glistening and contained no excess fluid. The pericardial sac was smooth and glistening and showed no gross lesions. The heart was not weighed, but its size seemed normal. The epicardial surface showed no gross abnormalities, and the color of the myocardium beneath it was a normal red-brown. The great vessels arose from their normal positions. When the heart was opened, the myocardium and the endocardial surfaces showed no abnormalities. The valves were thin and transparent; the papillary muscles were normal in size, and the chordae tendinae were long and thin. The ductus arteriosus was obliterated, and the foramen ovale was closed.

The lungs were not weighed but appeared normal in size. They were of increased consistency throughout, and a small nodule was palpated on the posterior surface of the upper lobe of the right lung. On section, severe bronchopneumonia was revealed throughout both lungs. The nodule in the upper lobe of the right lung measured 1 cm. in diameter and was grayish white and fleshy. The mediastinal nodes were greatly enlarged; they were firm and discrete and on section were a pale ivory color.

The spleen weighed 60 Gm; it had a smooth red-blue surface and on section a firm purple-red pulp. There were no gross lesions.

The liver weighed 330 Gm. and was smooth, red-brown and firm. On section, numerous miliary nodules were found throughout the hepatic tissue. These nodules were light gray and measured as much as 5 mm. in diameter. The hepatic ducts, cystic duct and common bile ducts were all patent and showed no abnormalities. The gallbladder was small and thin walled and presented nothing of note.

In the lower portion of the esophagus and stomach, the mucosal pattern was normal and no gross abnormalities were found. The mucosa throughout the entire small intestine was distinctly roughened and coarse. The large intestine was normal throughout.

The kidneys were not weighed, but they were of normal size and consistency. The capsules were stripped with ease, and normal fetal lobulations and smooth red-brown surfaces were revealed. The corticomedullary markings were distinct, and no gross lesions were observed.

The retroperitoneal and mesenteric lymph nodes were enlarged. They were discrete and firm and on section appeared light gray. There was, however, no caseation necrosis.

The pancreas was normal in size, pink and firm, and showed no gross abnormalities. The adrenal glands were of normal size and color and on section revealed no gross lesions. The thymus and organs of the neck were normal. The head was not examined.

Microscopic Examination.—Liver: Where the liver was examined under low magnification, coarse portal cirrhosis was observed (fig. 1). The portal septums were wide, and the hepatic lobules were compressed. Under high magnification there were large numbers of macrophages throughout the portal tissue and between the hepatic cords. The hepatic cords were interrupted in many places by nests of macrophages (fig. 2). After the section was stained with the Gram-Weigert stain (fig. 2), all the macrophages were seen to be filled with Histoplasma capsulatum.

Lungs: In the upper lobe of the right lung there was one rather large nodule which resembled the smaller nodules from the lymph nodes, shown in figure 3. The center was necrotic, and the periphery was formed by

small epithelioid cells. Throughout the pulmonary tissue were many parasitized macrophages in the alveoli and the interalveolar septums.

Small Intestine: The mucosa in the lower part of the ileum was thickened and velvety. On microscopic examination the villi were found to be altered distinctly. They were short and thick; the covering epithelium

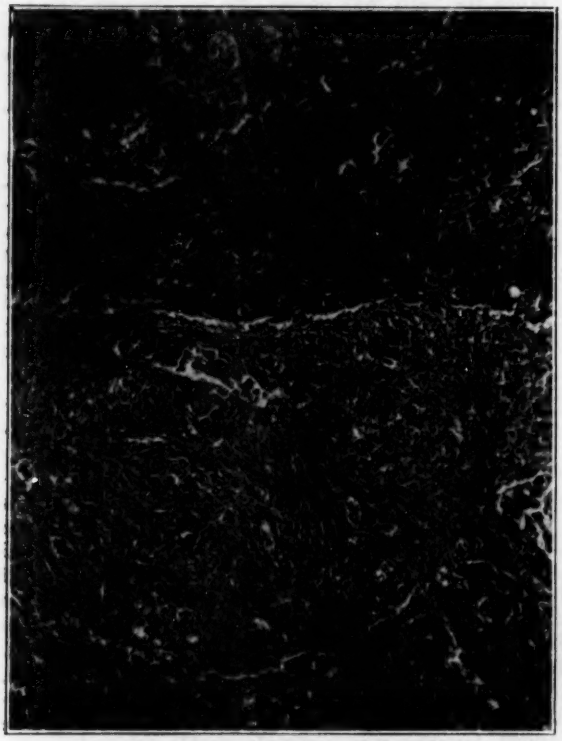

Fig. 1.—Cirrhosis of the liver (hematoxylin and eosin stain; low power field).

was absent, and the normal structure was lost completely, in that nothing was visible except closely packed parasitized macrophages (fig. 4). The destruction of the villi afforded a satisfactory explanation of the diarrhea. The changes in the rest of the small intestine were in general similar to those in the ileum.

Lymph Nodes: The structure of the lymph nodes was altered completely. In part they were made up of numerous small tubercles with caseous central necrosis (fig. 3). The peripheries of the tubercles were composed of small epithelioid cells. In other areas of the nodes (fig. 5) parasitized macrophages had replaced nearly all the normal tissue. Sinusoids and lymphoid cords were no longer recognizable.

The adrenal medulla was replaced largely by parasitized macrophages. The spleen showed no changes other than congestion of the pulp. There were occasional macrophages filled with parasites in the myocardium. No microscopic changes were found in the kidneys, uterus, uterine tubes, ovaries or pancreas.

SUMMARY OF CASES FROM THE LITERATURE

A brief summary of each of the other cases, arranged in order of age of the patient at the time of admission to the hospital, follows:

CASE 2 (reported by Schlumberger and Service [11a] in 1944, from Philadelphia).—The infant, a white boy, was admitted to the hospital at the age of 7 weeks, for treatment of hydrocele of the right testis. On admission physical examination revealed an irritable, pale child with a temperature of 101.4 F., abdominal distention, splenomegaly, hepatomegaly and harsh breath sounds but with no changes on percussion and no rales in the lungs. While in the hospital, the infant had increasing dyspnea and anorexia. He frequently regurgitated feedings and often had attacks of cyanosis with the feeding. His temperature ranged between 100 and 102 F. Minute petechial hemorrhages appeared on the buttocks and the chest. On the sixteenth day after admission splenic puncture was performed, and smears stained with Wright stain revealed Histoplasma capsulatum. On the seventeenth day, the organism was found in the marrow of the tibia. Blood agar plates were cultured from both the spleen and the bone marrow, and the organisms were isolated in pure culture subsequently. The infant died on the eighteenth day after admission, at the age of 9½ weeks. On admission the erythrocyte count was 2,400,000, the value of hemoglobin was 7.5 Gm., platelets numbered 97,000 and leukocytes numbered 6,100, with 20 per cent neutrophils, 77 per cent lymphocytes and 3 per cent monocytes. Anisocytosis, poikilocytosis and the presence of a few normoblasts were noted. The urine was normal. The Wassermann reaction of the blood was negative. Cultures of the stools

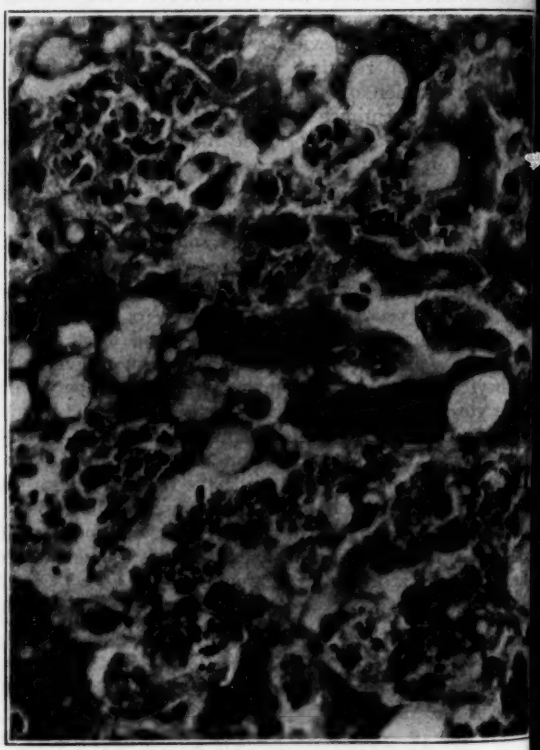

Fig. 2.—Organism in macrophages in liver (Gram-Weigert stain; high power field).

yielded no special pathogenic organisms. A roentgenogram of the chest showed nothing abnormal. Studies of the bone marrow on the seventh day after the infant's admission to the hospital disclosed no organisms. At necropsy, four well circumscribed yellow nodules 3 to 8 mm. in diameter were found in the lower lobe of the right lung. Microscopically, they resembled those observed in our case. The spleen weighed 80 Gm. and

he liver weighed 160 Gm., but neither showed any gross lesions. Microscopically, the lymph nodes, liver, spleen, lungs, skin, gastrointestinal tract, adrenal glands, thymus, bladder and bone marrow were invaded by macrophages laden with Histoplasma capsulatum.

CASE 3 (reported by Amolsch and Wax [11b] in 1939, from Detroit).—A white baby girl was admitted to the

Fig. 3.—Areas of caseation necrosis in lymph node (hematoxylin and eosin stain; low power field).

ospital at the age of 9 weeks, because of a chronic aroxysmal cough, which had begun shortly after birth. Chronic otitis media of the left ear soon developed; the nfant became pale, and her abdomen became distended. While she was in the hospital, a diagnosis of anemia econdary to infection was made. A roentgenogram of he chest showed some bilateral hilar peribronchial in-iltration. She continued to have fever, paroxysmal oughing and weakness. The abdominal distention was ound to be due to hepatosplenomegaly.

Laboratory studies revealed 2,000,000 erythrocytes per ubic millimeter and an average of 1,500 leukocytes, with rom 45 to 55 per cent neutrophils, 40 to 60 per cent ymphocytes and 2 to 12 per cent monocytes. The alue for hemoglobin was less than 50 per cent. Because f the clinical observations, a diagnosis of splenic anemia vas made, and splenectomy was done. After this, the umber of erythrocytes increased to 3,500,000, the con-entration of hemoglobin increased to 60 per cent and he number of leukocytes increased to 5,500. However, he clinical picture did not improve. The general ourse was downhill, and the child died three weeks fter the splenectomy, at the age of 8 months. Amolsch nd Wax stated that the disease lasted four months. Necropsy was not done. However, the spleen weighed 59 Gm. and was firm and grayish pink. On microscopic examination the splenic pulp was found to be engorged with large macrophages which were filled with Histoplasma capsulatum.

CASE 4 (reported by Rhodes, Conant and Glesne [11x] in 1941, from Cincinnati).—A white girl, 3 months of age, was admitted to the hospital with a history of regurgitation, fever and an impetiginous eruption on the skin of one month's duration. Physical examination revealed a pale, feverish infant with a crusted lesion on the left ear, hepatomegaly and splenomegaly. There was no adenopathy. While the child was in the hospital, purpuric lesions appeared on the umbilicus and back and erythematous lesions on the forearms. Cyanosis developed in association with bronchial breathing and rales in the lower lobe of the left lung. The infant failed to respond to treatment and died on the eighth day after admission to the hospital, at the age of 13 weeks. Laboratory observations revealed 2,720,000 erythrocytes and 7,300 leukocytes per cubic millimeter of blood, with 66 per cent neutrophils and 6 per cent large mononuclears. The value for hemoglobin was 7.1 Gm.; for serum cholesterol 99 mg. and for blood cholesterol 108 mg. per hundred cubic centimeter. Roentgenograms of the skull and long bones revealed no abnormalities. A postmortem blood culture was positive for Histoplasma capsulatum.

Fig. 4.—Villus of ileum showing complete destruction of normal structure and heavy replacement by parasitized macrophages (hematoxylin and eosin stain; high power field).

The important gross lesions found at necropsy were a large soft spleen, generalized consolidation of the lungs and a large, friable, golden yellow liver. Microscopically, the lymph nodes, spleen, lungs, liver, kidney and pancreas showed macrophages which were filled with Histoplasma capsulatum. No areas of necrosis were observed.

CASE 5 (reported by Parsons and Zarafonetis [11h'] in 1945, from data supplied by Dawson, in Tennessee).—The patient was a white boy, 3 months of age. Vomiting occurred, and hepatosplenomegaly and lesions in his mouth were noted. The laboratory studies revealed 1,500,000 erythrocytes, 2,000 to 4,000 leukocytes and a value for hemoglobin of 4.2 Gm. The duration of the illness was not stated. The diagnosis was established by necropsy and culture of the organism. The only lesions reported found at necropsy were in the gastrointestinal tract.

CASE 6 (reported by German, Ashmun and Dille [11n] in 1943, from Dayton, Ohio).—A white baby boy, 16 weeks of age, was brought to the hospital. He had had diarrhea, fever and abdominal distention for ten days. Physical examination revealed an extremely pale, fev-

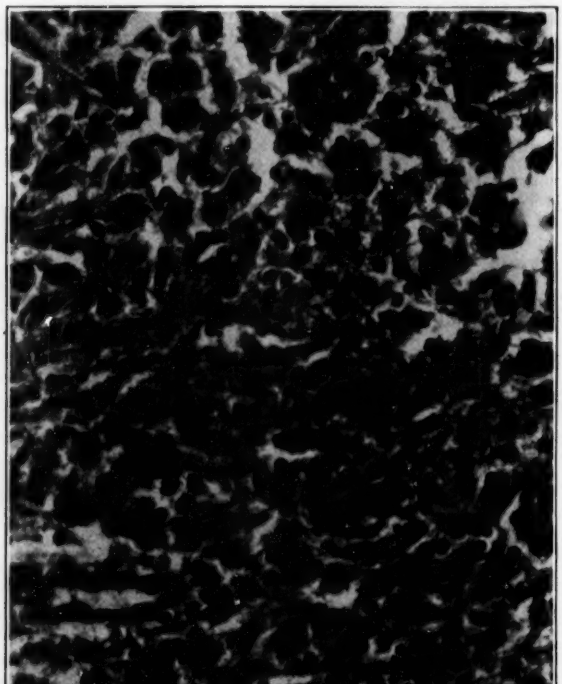

Fig. 5.—Replacement of normal tissue of lymph node by parasitized macrophages (hematoxylin and eosin stain; high power field).

erish (temperature 103 F.), well nourished, well developed infant with evident splenomegaly and hepatomegaly but no adenopathy. The examination was otherwise noncontributory. The general course was downhill, and, in spite of transfusions, the infant died on the tenth day after admission to the hospital.

The value for hemoglobin was 6 Gm.; erythrocytes numbered 1,900,000 and leukocytes 5,100, of which 28 per cent were neutrophils and 72 per cent lymphocytes. There were 6 normoblasts. Study of the blood revealed anisocytosis, poikilocytosis, polychromatophilia and basophilic stippling. No parasites were found in the blood smear, and cultures of blood and feces were also negative for Histoplasma capsulatum. The leukocyte count varied from 1,500 to a terminal count of 22,500.

At necropsy only hepatomegaly and splenomegaly were noted. Microscopically, Histoplasma capsulatum was found in lungs, heart, thymus, spleen, lymph nodes, kidneys and liver.

CASE 7 (reported by Parsons and Zarafonetis [11h'] in 1945, from data supplied by Poncher in Illinois).—A white girl, 4½ months old, had diarrhea, fever (temperature 102 F.) and hepatosplenomegaly. Laboratory studies revealed 2,600,000 erythrocytes, 4,400 leukocytes and 7.8 Gm. of hemoglobin. The duration of the disease was two and a half months. The diagnosis was established at necropsy, which revealed lesions in the gastrointestinal tract, lungs, lymph nodes, adrenal glands and thymus.

CASE 8 (reported by Hild [11r] in 1942, from Nashville, Tenn.).—A white girl, approximately 21 weeks old, was brought to the hospital. She had had a normal birth and no disturbances until one week before admission, at which time she became irritable and her rectal temperature rose to 103 F. The family physician noted pallor, splenomegaly and hepatomegaly. Studies of the blood revealed anemia. The pertinent clinical observations on admission were rectal temperature of 102.2 F., pulse rate of 146 beats per minute, respiratory rate of 42 per minute, pallor, crying when picked up, submaxillary and inguinal adenopathy, injection of the left tympanum, congestion of the nasopharynx, decreased resonance and breath sounds in the right side of the chest and abdominal distention with hepatomegaly and splenomegaly. The clinical diagnosis was bilateral catarrhal otitis media, bronchopneumonia and anemia. Transfusions of blood, gavage and administration of sulfathiazole were used in treatment.

Laboratory observations revealed 4,850,000 erythrocytes, 721,000 platelets and 7,650 leukocytes, of which 44 per cent were neutrophils and 52 per cent lymphocytes. The value for hemoglobin was 44 per cent. The urine was normal. The Kahn and Mantoux reactions were negative. Two cultures of blood were discarded as negative after five days. Blood smears revealed no organisms. Agglutination did not occur for organisms of the typhoid group and Brucella. Biopsy of sternal marrow revealed Histoplasma capsulatum. Antimony compounds were given, but the general course was downhill, and the infant died thirty-one days after admission, at the age of 184 days (26 weeks). During the last week of life gangrenous regions developed on the skin of the left buttock, abdomen and left thigh. The abdomen became noticeably distended. The child was dyspneic, and rales were heard in the bases of the lungs.

The important gross lesions found at necropsy were nodular lesions at the hilus and periphery of the right lung, enlargement of hilar nodes, noticeably enlarged thymus, granulomatous nodules in Peyer's patches, enlarged mottled liver and enlarged flabby spleen. Microscopic examination revealed granulomatous nodules in the lungs and in the hilar and abdominal lymph nodes, caseation necrosis of the adrenal glands, thymus and bone marrow; involvement of the liver, spleen and kidneys, and ulceration of the small bowel.

CASE 9 (reported by Dodd and Tompkins [10] in 1934 from Nashville, Tenn.).—A white boy, aged 6 months, was admitted to the hospital with a history of being well until three weeks before admission, when an infection of the upper respiratory tract developed. One week later paroxysmal coughing and vomiting began. Two days before admission a "lump" was noted in the abdomen. The pertinent observations on admission to the hospital were pallor, weakness, hepatomegaly, splenomegaly and anemia. The rectal temperature was 100 F. and the pulse rate was 140 beats per minute. The liver and spleen increased in size; jaundice and gen-

eralized edema developed, and the patient became dyspneic. The general course was downhill, and the child died at the age of 6½ months, thirty-three days after symptoms first appeared.

Laboratory studies in the hospital revealed 2,070,000 erythrocytes, 6.4 Gm. of hemoglobin and 17,700 leukocytes, with moderate lymphocytosis. The carbon dioxide–combining power of the plasma was 18.6 per cent; the p_H of the blood was 7.04 and the value for serum albumin was 2.4 per cent and for serum globulin 1.9 per cent. The icterus index was 30; the van den Bergh reaction was immediate and direct, and urinalysis gave essentially normal results. A blood smear before death revealed Histoplasma capsulatum in large mononuclear cells.

The pertinent gross observations at necropsy were a large necrotic liver and spleen, heavy noncrepitant lungs and enlarged, pale mesenteric, periaortic and peribronchial lymph nodes. Microscopically, the liver showed central lobular necrosis and engorgement of the sinusoids with parasitized macrophages. In the lungs several granulomatous nodules were associated with a massive infiltration of mononuclear cells. The sinusoids of the spleen were engorged with macrophages laden with parasites. There were granulomatous lesions of the lymph nodes and less severe involvement of the bone marrow, brain, intestinal mucosa and skin.

CASE 10 (reported by Parsons and Zarafonetis [11h'] in 1945, from data supplied by Dawson, in Tennessee).—The patient, a white girl 6 months old, had cervical and inguinal lymphadenopathy, hepatosplenomegaly and slight anemia. The duration of the disease was one month. Diagnosis was made by biopsy of sternal marrow and by culture. Necropsy revealed lesions of the gastrointestinal tract, lungs, bone marrow and thymus.

CASE 11 (reported by Agress and Gray [11a] in 1939, from St. Louis).—A white boy, 7 months of age, who had failed to gain weight and had had recurrent epistaxis, night sweats and sores about the lips of one month's duration, was admitted to the hospital. The infant appeared pale, malnourished and underdeveloped. His temperature was 102 F. There was a saddle type of nose, with perforation of the nasal septum and mucopurulent rhinitis. The percussion note and breath sounds were reduced posteriorly; the edge of the liver was palpable 2 fingerbreadths below the right costal margin, and there was pronounced splenomegaly. There were several anal fissures. A tentative diagnosis of congenital syphilis was made, and the patient was treated with arsenicals. However, he failed to respond to treatment, became progressively worse and died on the nineteenth day after admission to the hospital, at the age of approximately 31 weeks, seven weeks after the onset of the disease.

Laboratory examination revealed 3,140,000 erythrocytes, 66 per cent hemoglobin and 5,850 leukocytes, with 51 per cent neutrophils, 42 per cent lymphocytes and 7 per cent monocytes. Cultures of blood, spinal fluid and materials from the nasopharynx were all negative for pathogenic organisms. Blood smears gave evidence of a mild regenerative anemia but no thrombopenia. Roentgenograms of the chest showed increased pulmonary fibrosis. The diagnoses considered were congenital syphilis, obscure malignant disease, undetermined blood dyscrasia, bronchopneumonia, sepsis and rickets.

At necropsy the pertinent gross abnormalities were ulceration of the mouth; anal fissures; numerous minute yellowish myocardial nodules; firm, gray, irregularly consolidated lungs; spleen enlarged to twice normal size; hepatomegaly, and many tiny fresh superficial ulcerations throughout the large bowel. Microscopic study revealed generalized pulmonary invasion by Histoplasma capsulatum in large macrophages, with tumor-like projections into lumens of the arterioles; massive replacement of the mesenteric lymph nodes by macrophages laden with parasites, and numerous necrotic lesions. There was periportal infiltration of the liver with macrophages containing parasites, but the portal connective tissue was increased only slightly. Generalized involvement of the spleen without necrosis and ulcers in the large bowel extending into the follicles were noted.

CASE 12 (reported by Anderson, Michelson and Dunn [11c] in 1941, from St. Louis).—A white girl, 8 months of age, was brought to the hospital with a history of infection of the upper respiratory tract of four months' duration. Two months after the onset of the infection mild diarrhea developed and persisted for three weeks. Just before admission, after administration of sulfanilamide, a generalized purpuric rash developed. The pertinent physical observations on admission were a temperature of 101 F., otitis media, hepatosplenomegaly and cervical adenopathy. The child's temperature ranged between 99 and 104 F. Several days after admission the right tympanum perforated and freed a thick purulent exudate. The patient did not respond to supportive treatment with blood transfusions, vitamins and liver extract and died two weeks after admission to the hospital, approximately four months after the symptoms began.

Laboratory observations disclosed between, 1,880,000 and 3,880,000 erythrocytes and between 1,850 and 2,500 leukocytes per cubic millimeter of blood, of which between 62 and 80 per cent were lymphocytes. Thrombopenia was pronounced, with a bleeding time of eighteen minutes and a coagulation time of four minutes. Several cultures of blood and blood smears were negative for organisms. A roentgenogram of the chest revealed tuberculosis of the right hilar region and bronchitis associated with early bronchopneumonia.

At necropsy the pertinent gross observations were moderate generalized lymphadenopathy, hepatomegaly (weight 450 Gm.), splenomegaly (weight 94 Gm.) and small ulcers in the large intestine. Microscopic examination revealed parasitization of macrophages in the lymph nodes, thymus, lungs, spleen, liver, bone marrow, endothelium of blood vessels, renal glomeruli and large intestine. Widespread patchy interstitial pneumonitis with occasional areas of coagulative necrosis and macrophages laden with parasites were noted in the lungs. Except for the more extensive involvement, the picture resembled that in previous cases.

CASE 13 (reported by Beamer, Smith and Barnett [11d] in 1944, from St. Louis).—A white boy, 10½ months old, was admitted to the hospital because of fever, cough and dyspnea of one week's duration. Prior to this illness the patient had been well except for impetigo, which had been present since birth and had failed to clear completely. The pertinent observations on admission were fever (103.3 F. [39.6 C.]), semicoma, irritability, restlessness, generalized encrusted vesicular dermatitis, petechial hemorrhages, cyanosis, irregular grunting respirations, moist cough, congestion of the nasopharynx and the tympanic membranes, roughened pulmonary breath sounds, hepatomegaly, splenomegaly and questionable nuchal and spinal rigidity.

Laboratory examination revealed 3,600,000 erythrocytes and 16,000 leukocytes, of which 86 per cent were neutrophils (25 per cent juvenile cells, 55 per cent stab cells and 6 per cent segmented forms). The spinal fluid was clear and sterile bacteriologically, with a cell count of 4. The carbon dioxide–combining power was 48 volumes per cent. The value for non-

protein nitrogen was 35.5 mg. per hundred cubic centimeters, for serum chlorides (as sodium chloride) 540 mg. per hundred cubic centimeters and for serum dextrose 86 mg. per hundred cubic centimeters. Cultures of materials from the throat and of blood were positive for hemolytic staphylococci. The infant's course was steadily downhill, and he died thirteen and a half hours after admission.

At necropsy the pertinent gross observations were numerous firm irregular yellow-gray masses, 1 to 10 mm. in diameter, throughout the lungs; generalized lymphadenopathy, with grayish necrotic centers; hepatomegaly (weight 355 Gm.); splenomegaly (weight 75 Gm.); firm yellowish nodules in the liver, spleen and kidneys; studding of the mucosa of the appendix and cecum with soft gray elevated masses, and firm gray masses in the pleura, peritoneum and pericardium. Microscopically, there were macrophages filled with parasites in the lungs, lymph nodes, liver, spleen, pancreas, adrenal cortex and kidneys, ulceration of the colon and masses in the serous membranes and in the bone marrow.

CASE 14 (reported by Shaffer, Shaul and Mitchell[11y] in 1939, from Virginia).—A white girl, about 11 months of age, was admitted to the hospital. The illness had begun five months earlier with intermittent fever and projectile vomiting. One month before admission fever, drowsiness and alternating periods of diarrhea and constipation occurred. The pertinent observations on admission were malnourishment, dehydration, fever (temperature 103.2 F.), cervical adenopathy, hepatosplenomegaly, small elevated white lesions of the skin over the left costal region, tachycardia and a pulmonic systolic murmur. A diagnosis of aleukemic leukemia was made. The patient's course was downhill, and she failed to respond to supportive treatment. Her temperature remained elevated, and terminally ulcerative, purpuric decubitus lesions developed in the skin and gangrenous lesions in the ala of the nose. The patient died on the twenty-second day after admission, seven months after the illness began. She was then 12½ months old.

Laboratory examinations revealed 2,140,000 erythrocytes on admission and 2,900,000 at the time of death, 3,700 leukocytes on admission and 2,500 at the time of death and 5 Gm. of hemoglobin on admission and 9.5 Gm. at time of death. Differential leukocyte counts revealed 64 per cent neutrophils, 32 per cent lymphocytes and 4 per cent monocytes. The urine was normal. The Schick, Wassermann and Kahn tests elicited negative reactions. Blood smears indicated moderate anisocytosis but no parasites.

At necropsy the pertinent gross observations were a large, firm congested liver (weight 237 Gm.), splenomegaly (weight 144 Gm.), ulceration of the intestinal mucosa, mesenteric lymphadenopathy and gray-white nodular lesions of the cortices of the kidneys, Microscopic examination revealed granulomatous lesions in the liver, spleen, kidneys, mesenteric nodes, small bowel and adrenal glands and less severe involvement of the pancreas and bone marrow with Histoplasma capsulatum. The lungs, peribronchial nodes and thymus were all normal.

CASE 15 (reported by Scott[11a'] in 1941, from Louisville, Ky.).—A Negro boy, 15 months old, was admitted to the hospital. He had an attack of "pertussis" three months prior to admission, which lasted approximately six weeks. One month before admission he became feverish and began to lose weight rapidly. The pertinent physical observations on admission to the hospital were fever (temperature 104 F.); abdominal distention; hot dry skin; cervical, axillary and inguinal adenopathy; dulness at the bases of both lungs, and hepatosplenomegaly.

Laboratory studies revealed less than 7.5 Gm. of hemoglobin, 2,460,000 erythrocytes and 4,100 leukocytes, of which 60 per cent were neutrophils, 12 per cent lymphocytes and 6 per cent monocytes. The number of erythrocytes decreased to 1,890,000 and of leukocytes to 2,900; the concentration of hemoglobin remained less than 7.5 Gm. Urinalysis revealed albuminuria, grade 1 plus, a few granular casts, 6 to 8 leukocytes, many bacteria and a positive culture for Staphylococcus aureus. The icterus index was 12, and the value for bilirubin was 0.2 mg. per hundred cubic centimeters. Cultures of materials from the throat were negative for pathogenic organisms. No active pathologic lesions were visible in the roentgenograms of the chest, but just before death shadows were suggestive of tuberculosis. Roentgenograms of the skull showed nothing abnormal. The general course in the hospital was downhill. The patient terminally became dyspneic, restless and irritable. He died on the nineteenth day after admission, at the age of approximately 16 months. His death occurred seven weeks after the onset of symptoms.

At necropsy the pertinent observations were hepatomegaly, splenomegaly (weight 85 Gm.), mesenteric adenopathy, hyperplasia of Peyer's patches, ulceration of intestinal mucosa and white granulomatous lesions, 2 mm. in diameter throughout the lungs.

On microscopic examination, caseation necrosis was found in the granulomas in the lungs and in the spleen, abdominal lymph nodes and liver, together with hyperplasia of the bone marrow. All these organs were engorged with macrophages containing Histoplasma capsulatum.

CASE 16 (reported by Villela and Pará,[6] from Brazil; cited by Meleney in 1940).—The child was a 3 year old, white girl, who had a febrile illness for two months. Biopsy of the liver revealed Histoplasma capsulatum. Nothing else was reported.

CASE 17 (reported by Parsons and Zarafonetis[11b'] in 1945 from data supplied by Moore in Missouri).—The patient was a white girl 4 years old. On examination she showed signs of pneumonia, fever, anorexia, lymphadenopathy and hepatosplenomegaly. Laboratory studies revealed 2,760,000 erythrocytes, 1,800 to 6,600 leukocytes and 5.3 Gm. of hemoglobin. The duration of the disease was five weeks. The diagnosis was established at necropsy and from culture of blood. Necropsy revealed lesions of the gastrointestinal tract, skin, lungs, lymph nodes and bone marrow.

CASE 18 (reported by Müller,[6] from East Java, in 1931; cited by Meleney in 1940).—The patient was a Javanese Negro, 7 years of age, who had had a long history of fever, emaciation, diarrhea and generalized lymphadenopathy. At necropsy the intestinal mucosa was ulcerated and involvement with Histoplasma capsulatum was generalized.

CASE 19 (reported by Meleney in 1940, from data from Indiana, supplied by Forry and Culbertson[6]).—A white boy, 10 years old, from Indiana, presented a picture of acute sepsis associated with generalized lymphadenopathy and splenomegaly. Necropsy revealed ulceration of the ileum and colon and generalized

involvement of the organs of the body with typical lesions of histoplasmosis.

CASE 20 (reported by Meleney in 1940, from data from Ohio supplied by Weller).[6]—A white boy, 12 years old, had died. The diagnosis of aplastic anemia was made. Four years later, reexamination of a lymph node by Dr. Weller revealed large macrophages engorged with Histoplasma capsulatum.

CASE 21 (reported by Parsons and Zarafonetis in 1945, from data supplied by Gray, in Missouri).—The patient was a boy whose age was not given. He had cervical adenopathy, which on biopsy revealed the organisms. No other data were given.

CLINICAL AND PATHOLOGIC FEATURES OF HISTOPLASMOSIS IN CHILDREN

The cases of 21 children less than 13 years of age, 15 of whom were 15 months of age or less, have been reported.

limits are indicated. Twelve of the children were 8 months of age or less.

The disease lasted from one week to seven months; the average duration was around three months.

In adults, the disease may appear as localized nodules or ulcers in the skin or the mucous membranes. More often the features are those of a systemic infection with special involvement of some organs, such as the lungs, gastrointestinal tract, heart and joints.

In infants, the symptoms are different. They consist of fever, pallor, diarrhea, failure to gain or actual loss of weight, difficulty in feeding, chronic cough, irritability, abdominal distention, cyanosis with feeding, hepatomegaly, splenomegaly, lymphadenopathy, purpura, anemia and leukopenia.

Incidence According to Age, Sex and Color in Twenty-One Cases of Histoplasmosis in Children

The cases are arranged according to the age of the patient at the time of his admission to the hospital

Reported by	Date	Country or State	Age*	Sex	Color or Race
Schlumberger and Service	1944	Pennsylvania	7 weeks	Male	White
Tams, Tenen and Flanagan	1945	Minnesota	3 months†	Female	White
Amolsch and Wax	1939	Michigan	9 weeks	Female	White
Rhodes, Conant and Giesne	1941	Ohio	3 months	Female	White
Parsons	1945	Tennessee	3 months	Male	White
German, Ashmun and Dille	1942	Ohio	16 weeks	Male	White
Parsons	1945	Illinois	4½ months	Female	White
Hild	1942	Tennessee	21 weeks	Female	White
Parsons	1945	Tennessee	6 months	Female	White
Dodd and Tompkins	1934	Tennessee	6 months	Male	White
Agress and Gray	1939	Missouri	7 months	Male	White
Anderson, Michelson and Dunn	1941	Missouri	8 months	Female	White
Beamer, Smith and Barnett	1944	Missouri	10½ months	Male	White
Shaffer, Shaul and Mitchell	1939	Virginia	11 months	Female	White
Scott	1941	Kentucky	15 months	Male	Negro
Meleney	1940	Brazil	3 years	Female	White
Parsons	1945	Missouri	4 years	Female	White
Müller	1932	Java	7 years	Male	Negro
Meleney	1940	Indiana	10 years	Male	White
Meleney	1940	Ohio	12 years	Male	White
Parsons	1945	Missouri	Not stated	Male	White

* Age at time of admission to hospital.
† Age at time of onset of the disease was 8 weeks.

Only 2 of the 21 patients lived outside the United States. This, however, is not a true picture of the distribution of the disease, for in the 81 cases reported among patients of all ages the distribution has been worldwide. In the United States, the disease is widespread, having been reported in twenty-one states. Most of the 19 cases reported among children from the United States were from the North Central Region (table).

The youngest patient was that of Schlumberger and his associates [11a]; at the time of admission to the hospital he was 7 weeks old. In an effort to find a basis for comparison, the ages stated in the summaries are those at which the patients were admitted to the hospital. In spite of the inaccuracies of this method, the general age

Résumé of the Clinical and Pathologic Features in 21 Cases.—Skin: Clinically, cutaneous lesions were present in 4 cases. These consisted of crusted, vesicular, pustular, scaly and gangrenous lesions. Their distribution over the body was widespread, and only one type of lesions was noted in each case. In all these cases a generalized systemic infection was associated. In none of the reports was histology of the cutaneous lesions described. In 3 cases in which cutaneous lesions were not present Histoplasma capsulatum was noted on microscopic examination after death of the patient in the mononuclear cells of the loose areolar subcutaneous tissue. Purpuric lesions of skin were noted in 5 cases.

In case 9, the perforated nasal septum was found on microscopic examination to be invaded by Histoplasma capsulatum. This is the only reported instance of involvement of the mucous membranes in children, although such involvement is common in adults.

Respiratory Tract: Two patients had chronic colds but did not have gross lesions of the upper respiratory tract.

Pulmonary symptoms, such as dyspnea, cough and cyanosis, were present in 4 cases. In 2 of these, the cough was paroxysmal and associated with vomiting; thus the condition simulated pertussis. Six patients had signs of disease in the chest. These consisted of rales and decrease in breath sounds and percussion notes at the bases of the lungs. Roentgenograms of the chest revealed nothing abnormal in 4 of these cases, but in the fifth pulmonary fibrosis and bronchopneumonia were diagnosed from the roentgenogram. In 2 cases roentgenograms of the chest revealed involvement of the lungs in the absence of clinical data. In 15 cases lesions were found in the lungs at postmortem examination. The pulmonary lesions were sometimes in the form of multiple caseous nodules, but often they consisted of macrophages laden with Histoplasma capsulatum which were distributed diffusely throughout the parenchyma.

Gastrointestinal Tract: Nine patients had gastrointestinal symptoms. These symptoms were lack of appetite, regurgitation, cyanosis with feeding, vomiting, diarrhea, constipation and bulky stools. Diarrhea was the most prominent symptom in 4 cases. Roentgenographic studies of the colon revealed nothing abnormal in our case (case 1), and no roentgenographic studies of the gastrointestinal tract were reported in any of the cases surveyed. Cultures of stools were made and were negative for pathogenic organisms in 3 cases. In only 1 of these was the diagnosis of histoplasmosis made before necropsy.

Lesions were found in the gastrointestinal tract in 11 cases on gross examination. These usually consisted of ulceration of the mucosa of the ileum and large bowel. In 1 case granulomatous nodules were found on the mucosal surface of the ileum, and in several cases Peyer's patches were prominent. Our case was the only one in which the changes in the mucosa of the ileum were striking on gross examination. Gross lesions were found at necropsy in only 5 of the 9 cases in which intestinal symptoms were present. Diarrhea was the main symptom referable to the gastrointestinal tract in 4 of these 5 cases. The massive involvement of the villi in our case must have interfered with intestinal absorption and presumably caused the diarrhea. In 5 cases in which gross intestinal lesions were found at necropsy, symptoms referable to the intestinal tract had not been present.

Involvement of the gastrointestinal tract was observed on microscopic examination in 13 cases. In the majority of these cases the lesion consisted of ulceration of the mucosa with minimal invasion of the lymph follicles. In only 2 cases was involvement of the mucosa and submucosa severe. Granulomatous lesions or caseation necrosis was not found in the gastrointestinal tract in any case.

Spleen: Splenomegaly was found in 17 cases. The lower border of the spleen was from 1 to 8 cm. below the left costal margin in these cases. Gross lesions due to Histoplasma capsulatum were found in only 1 of these cases. These consisted of several pale caseous nodules throughout the organ. The weight of the spleens ranged from 80 to 159 Gm., but because of differences in ages the weight was not a true index of the enlargement. However, the spleens were usually three to four times normal size. Microscopically the splenic parenchyma was involved in 13 cases. The usual picture was invasion of the pulp and sinusoids by macrophages laden with parasites. Granulomatous lesions were noted in the splenic pulp in only 3 cases; in 1 of these there was caseation necrosis.

Lymph Nodes: Generalized lymphadenopathy was reported as a clinical observation in 9 cases. Usually the nodes were firm, discrete, painless and only moderately enlarged. Adenopathy was found at necropsy in 15 cases. The periaortic, mesenteric and mediastinal nodes were involved most often and most severely. The typical lesion on section presented a gray-yellow caseous surface which was much like that of a tuberculous lymph node. Microscopically, the normal architecture was replaced by myriads of macrophages containing parasites and numerous areas of caseation necrosis without epithelioid cells or Langhans' giant cells.

Liver: Hepatomegaly was reported as a clinical observation in 16 cases. The enlargement varied. The edge of the liver was palpable from 1 to 3 fingerbreadths below the right costal margin. Icterus was reported in 2 cases. In both of these the van den Bergh reaction was immediate and direct, and in 1 case (case 1) the concentration of serum bilirubin was 3.2 mg. per hundred cubic centimeters. The icterus index in the other was 30. These tests indicate hepatic damage. In

case, in which the icterus index was 30, there was anasarca and values for the serum proteins were as follows: albumin, 2.4 Gm. per hundred cubic centimeters, and globulin, 1.9 Gm. per hundred cubic centimeters.

Hepatomegaly was noted at necropsy in 15 cases, in 2 of which multiple caseous nodular lesions extended throughout the hepatic parenchyma. In no case other than ours (case 1) were cirrhotic changes reported. On microscopic examination involvement of the liver was reported in 14 cases. The usual picture corresponded to that described in our case, namely, invasion of the portal tissue and sinusoids by macrophages laden with parasites, hyperplasia of the portal connective tissue and atrophy of the hepatic lobules. Granulomas were found in a few instances.

Kidneys: Minimal albuminuria, pyuria and occasional casts were reported in a number of cases. However, in none did these appear to be clinically significant. No studies were made on the urine for Histoplasma capsulatum.

Gross renal lesions were observed in only 2 cases. These consisted of multiple small yellow-white nodular granulomas. Microscopically, these lesions resembled those in the liver, lungs and lymph nodes. In 4 other cases, the kidneys were reported to be involved on microscopic examination, but the involvement usually consisted of a minimal invasion of the renal parenchyma by parasitized macrophages.

Miscellaneous Lesions: Otitis media was observed in 3 cases, but no bacteriologic studies were made. On macroscopic examination the thymus was observed to be involved in 6 cases, the serous membrane in 1, the bone marrow in 4 and the adrenal glands in 6. Both the cortex and the medulla of the adrenal glands were invaded by parasitized macrophages, and a few granulomas were noted.

Microscopic examination revealed that the bone marrow was invaded by parasitized mononuclear cells in 9 cases. No granulomas or massive destruction of the marrow was described. In 4 of these cases biopsy of the marrow revealed Histoplasma capsulatum. The myocardium was found involved in 3 cases, the pancreas in 3, the bladder in 1, the cerebrum in 1 and the serous membranes in 1.

Blood: Clinical investigation of the blood usually revealed hypochromic normocytic anemia with associated leukopenia and in a few cases thrombopenia. Values for hemoglobin ranged from 4.2 to 8.4 Gm. and averaged 7.5 Gm. per hundred cubic centimeters. The number of erythrocytes ranged from 1,500,000 to 4,850,000 and averaged 2,500,000. Leukocyte counts ranged from 1,500 to 17,700. Definite leukocytosis was present in only 2 cases; in all other cases the leukocyte counts were less than 7,560.

Evidence of regeneration of erythrocytes, consisting of anisocytosis, poikilocytosis, polychromatophilia and basophilic stippling, was noted in 5 cases. The differential leukocyte count was indeterminate in nature, but in several cases revealed a relative lymphocytosis.

The parasite was observed in the macrophages in a blood smear in 1 case only. In 2 other cases in which such examination was reported, no organisms were found in the blood smear.

In 5 cases, the blood was sterile on culture. However, in none of these cases was the disease suspected, and as a result the cultures may have been discarded too soon. In 1 case staphylococci were reported in the blood, and in another Histoplasma capsulatum was cultured from the blood.

Other studies on the blood, such as determinations of the carbon dioxide–combining power and the values for cholesterol, nonprotein nitrogen and dextrose, did not reveal anything of clinical or diagnostic value.

DIAGNOSIS, PROGNOSIS AND TREATMENT

Although the clinical picture is variable and a definite diagnosis cannot be reached by clinical means alone, nevertheless, when a patient has a history of fever, loss of weight, feeding problems, chronic cold or cough and diarrhea with hepatomegaly, splenomegaly, adenopathy, hypochromic normocytic anemia and leukopenia, histoplasmosis should be considered as a definite possibility. Not all of the symptoms and clinical observations need to be present in any one case, and many more might be added. It is only by having histoplasmosis in mind that the proper laboratory tests can be made.

The procedures that may be of value in making the diagnosis are as follows: 1. Biopsy of lymph nodes, spleen, bone marrow or cutaneous lesions may provide information concerning the presence of the parasites. In 1 case the diagnosis was established before death as a result of splenic puncture and in 3 others as a result of biopsy of the bone marrow. We are of the opinion that the diagnosis can usually be made with the aid of biopsy. The Gram-Weigert stain is the best for demonstration of the parasites. 2. Blood smears are occasionally positive for Histoplasma. 3. Cultures of blood also should prove valuable if Sabouraud's medium (or blood agar) is used

and the culture is incubated for several weeks. However, the delay in establishing the diagnosis limits its usefulness. 4. A cutaneous test was described by Van Pernis, Benson and Holinger [11d] in 1941. Nothing further has been reported on this test, however, and its clinical value has not been determined.

The prognosis of histoplasmosis has been uniformly poor. Only 1 patient has been reported symptomatically cured. This patient was reported well four years after treatment. An antimony compound (Neostam [nitrogen glucoside of sodium paraaminophenyl stibonate]) was used in this case, but in other cases it has failed to affect the course of the disease. Sulfonamide compounds and supportive measures, such as transfusions, parenterally administered fluids and vitamins have been of no value.

Nothing is known as to the mode of entrance of the organism into the body. Intrauterine infection seems possible in those cases in which symptoms develop before the patient is 3 months old.

Assistance and advice were given by Dr. E. T. Bell, professor of pathology, School of Medicine, University of Minnesota, Minneapolis.

Obituaries

WILLIAM A. MULHERIN, M.D.
1872-1945

After a long life devoted to caring for the health of his own community and to the advancement of pediatrics all over the country, Dr. William Anthony Mulherin died of coronary thrombosis at Augusta, Ga., April 19, 1945.

Dr. Mulherin combined unusual personal charm with exceptional ability, great integrity and deep concern for the welfare of his fellow beings. A beloved friend and physician to his patients, he was a tireless worker for the proper care of all sick children. Not only did he practice pediatrics; he taught pediatrics, and he gave his time unstintingly to lecturing at medical society meetings throughout the country on scientific subjects related to pediatrics.

He was born in Augusta, Ga., July 3, 1872. He held the degrees of A.B. and A.M. from Spring Hill College, Mobile, Ala.; and of M.D. from Harvard Medical School, having been graduated there in 1901. He was professor of pediatrics for many years and professor emeritus of clinical pediatrics in the University of Georgia School of Medicine, and was serving as an acting professor there at the time of his death. Dr. Mulherin was an organizer and later a chairman of the pediatric section of the Southern Medical association, and one of the chairmen of the Section on Diseases of Children of the American Medical Association, acting as a member of the Abraham Jacobi Committee of this Section in 1922. He was appointed a member of President Hoover's Conference on Child Health and Protection and during 1942, 1943 and 1944, acted as a member of the House of Delegates of the American Medical Association. Among his honors were the honorary degree of Doctor of Sciences from University of Georgia, a fellowship in the American Academy of Pediatrics, membership in the American Pediatric Society, past presidency of the Georgia State Medical association, and the rank of dean emeritus of the Southern Pediatric Seminary. On the staff of the Wilhenford and University Hospitals, he also served as a member of Georgia State Board of Health, and as chairman of the Richmond County Board of Health.

News and Comment

GENERAL NEWS

Announcement of Certification in Allergy, by the American Board of Pediatrics, Inc. — The American Board of Pediatrics, Inc., at its last meeting, in New York city, took final action establishing certification in allergy as a subspecialty of pediatrics.

Certification in pediatrics by the American Board of Pediatrics, Inc., is a prerequisite for such certification in allergy. Those who are already specialists certified by the American Board of Pediatrics and who wish to be certified in allergy must make formal application to the Secretary of the American Board of Pediatrics, Inc., Dr. C. A. Aldrich, 115½ First Avenue, Southwest, Rochester, Minn. Those who are not yet certified in pediatrics and who desire certification in allergy as well should indicate this in their application to the American Board of Pediatrics, as examination in both subjects may be held at the same time.

The application fee for certification in allergy will be $25, in addition to the application fee for certification in pediatrics.

An Advisory Committee on Allergy has been appointed, to act with the American Board of Pediatrics in all matters pertaining to the selection and examination of applicants for subspecialty certification. This committee is identical with the Advisory Committee on Allergy of the American Board of Internal Medicine. The present members of this committee are:

Harry L. Alexander, M.D.
Robert A. Cooke, M.D.
Leslie N. Gay, M.D.
Harry L. Huber, M.D.
George Piness, M.D.
Francis M. Rackemann, M.D.

In December of this year, Dr. Oscar M. Schloss will be appointed as the pediatric member of this committee, to take the place of the retiring member.

The Advisory Committee on Allergy has already outlined the requirements for applicants who desire examination in the subspecialty of allergy, as follows:

1. Two years, full time, in a satisfactory allergy clinic and its hospital (including training in both allergy and pediatrics), or

2. One year, full time, in the allergy clinic and its hospital and two additional years of full attendance on such an allergy clinic and its activities, or

3. Five years, full attendance, on such an allergy clinic and its activities, or

4. Special training under qualified preceptors, solely or in combination with aforementioned types of training and such other training as may be felt adequate to prepare a person for the practice of allergy.

It is the further opinion of the Committee that clinics for such training should fulfil the following qualifications:

1. They should be in hospitals that have been accepted by the Council on Medical Education and Hospitals and by the American Board of Pediatrics, Inc., for training and certification in pediatrics and for residencies in pediatrics or medicine.

2. The Director of the Allergy Clinic shall be a specialist certified in allergy by the American Board of Internal Medicine or the American Board of Pediatrics.

When accepted, the candidate will receive from the American Board of Pediatrics, Inc., a certificate in allergy and will be listed as a specialist in allergy in the official directory of the Advisory Board for Medical Specialties.

Prospective applicants for certification in the subspecialty of allergy may apply to the Secretary of the American Board of Pediatrics, Inc., Dr. C. A. Aldrich, 115½ First Avenue, Southwest, Rochester, Minn., at any time after Nov. 1, 1945.

The Journal *The Nervous Child* Changes Hands —The journal *The Nervous Child* has been bought by its founder and editor-in-chief, Dr. Ernest Harms, from its previous owner, Grune & Stratton, Inc., medical publishers of New York. *The Nervous Child* will now be produced by a new publishing house, Child Care Publications, 30 West Fifty-Eighth Street, New York 19, which has been created for this purpose. The same publishing house will start to issue during 1946 another periodical, entitled *The Journal of Child Psychiatry*, devoted to unsolicited contributions in the field of mental disease in children.

CORRECTION

The publisher of "Microbial Antagonisms and Antibiotic Substances" by Selman A. Waksman, Ph.D., Sc.D., reviewed in the August issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN (**70**:129, 1945), is the Commonwealth Fund, not the Community Fund.

Abstracts from Current Literature

Vitamins; Avitaminoses

VITAMIN REQUIREMENTS IN INFANTS AND CHILDREN. J. R. VONACHEN, Illinois M. J. **86**:258 (Nov.) 1944.

This article consists of a résumé of present knowledge of the vitamin needs of infants and children, vitamin therapy and the author's interpretation of his experiences with use of the vitamins in his practice.

VARIATION IN THE ASCORBIC ACID REQUIREMENTS FOR SATURATION OF NINE NORMAL YOUNG WOMEN. ALICE B. KLINE and MARY S. EHEART, J. Nutrition **28**:413 (Dec.) 1944.

From their study of 9 young women, the authors found that 6 had a requirement of ascorbic acid for saturation of 1.4 to 1.8 mg. per kilogram of body weight; 1 required 0.6 mg. or less, and 2, 2.2 mg. or more. A simplified modification of the method using responses to the test dose for the determination of saturation needs of ascorbic acid was employed. Only the twenty-four hour samples of urine obtained before and after administration of the test dose were analyzed.

FREDEEN, Kansas City, Mo.

THE EFFECT OF SPRAY-DRYING AND THE SUBSEQUENT STORAGE OF THE DRIED PRODUCT OF THE VITAMIN A, D, AND RIBOFLAVIN CONTENT OF EGGS. CHARLES A. DENTON, C. A. CABELL, HARRY BASTRON and RUSSELL DAVIS, J. Nutrition **28**:421 (Dec.) 1944.

Denton and associates estimated the vitamin A content of emulsified whole eggs and spray-dried eggs by biologic and spectrophotometric methods, the vitamin D content by a biologic method and the riboflavin content by a microbiologic method. There was no loss of these vitamins during the spray-drying process. Riboflavin and vitamin D were stable in the stored dried products, and vitamin A was lost fairly rapidly, especially at the higher storage temperatures.

FREDEEN, Kansas City, Mo.

SOME FACTORS INFLUENCING THE FECAL ELIMINATION OF THIAMINE BY HUMAN SUBJECTS. ANNE WILLIAMSON and HELEN T. PARSONS, J. Nutrition **29**:51 (Jan.) 1945.

Stimulation of intestinal synthesis of thiamine was observed by Williamson and Parsons in their subjects with the ingestion of large amounts of plant fiber (pineapple), as noted by the relatively large fecal eliminations of thiamine. In general no correlation was found between variations in urinary and fecal output of thiamine for high and low fiber periods. Apparently, certain subjects destroyed considerable amounts of thiamine in the digestive tract.

FREDEEN, Kansas City, Mo.

EFFECTS OF LIGHT INTENSITY, DAY LENGTH, TEMPERATURE AND OTHER ENVIRONMENTAL FACTORS ON THE ASCORBIC ACID CONTENT OF TOMATOES. KARL C. HAMNER, LEON BERNSTEIN and L. A. MAYNARD, J. Nutrition **29**:85 (Feb.) 1945.

Hamner and associates studied the influence of environmental variables on the ascorbic acid content of tomatoes in the field and under controlled conditions in the laboratory. They concluded that the ascorbic acid content is only slightly, if at all, influenced by the degree of ripeness after the fruit is "mature green"; storage for ten to fourteen days at temperatures from 65 to 90 F.; fertilizer treatment of the plants (although nitrogen fertilization may cause a slight decrease), and relative humidity to which the plants are exposed.

Under controlled growing conditions fruits produced under lowered temperatures and shortened day length were somewhat lower in ascorbic acid. Light intensity prior to harvest had the greatest influence on the ascorbic acid content; this may be the dominant factor in determining the ascorbic acid content of ripe fruit.

FREDEEN, Kansas City, Mo.

THE NICOTINIC ACID, PANTOTHENIC ACID, CHOLINE AND BIOTIN CONTENT OF FRESH, IRRADIATED EVAPORATED AND DRY MILK. A. Z. HODSON, J. Nutrition **29**:137 (Feb.) 1945.

Hodson found that the average amount of nicotinic acid in fresh milk was 0.91 mg.; of pantothenic acid, 3.1 mg.; of choline, 149 mg., and of biotin, 47.1 mg., per liter. In the processing of irradiated evaporated, dry skim or dry whole milk, his data showed no significant losses in the contents of nicotinic acid, pantothenic acid, choline and biotin, with the possible exception of a slightly lowered biotin content of dry skim milk.

FREDEEN, Kansas City, Mo.

EFFECT OF SUNSHINE UPON THE ASCORBIC ACID AND RIBOFLAVIN CONTENT OF MILK. ARTHUR D. HOLMES and CARLETON P. JONES, J. Nutrition **29**:201 (March) 1945.

Holmes and Jones made a study of the effect on the ascorbic acid and riboflavin contents of exposing milk in commercial ½ pint (250 cc.) bottles to the action of sunshine. The destruction of reduced ascorbic acid was rapid, for little, if any, was present after thirty minutes' exposure; riboflavin disappeared more slowly. These data showed that milk allowed to stand for more than a short time on the consumer's doorstep exposed to strong light or sunshine is likely to lose a large amount of its ascorbic acid and riboflavin.

FREDEEN, Kansas City, Mo.

STUDIES ON CAROTENOID METABOLISM: V. EFFECT OF A HIGH VITAMIN A INTAKE ON THE COMPOSITION OF HUMAN MILK. M. CAROLINE HRUBETZ, HARRY J. DEUEL JR. and BERNARD J. HANLEY, J. Nutrition **29**:245 (April) 1945.

The administration of vitamin A in large doses effectively increased the vitamin A content of the milk of the lactating human subject in the same way as in the cow. Hrubetz and associates concluded that the administration of the large doses of vitamin A was not attended with any marked alterations in other components of the milk. There was no evidence of any deleterious effects of the vitamin A on the mothers or the offspring.

FREDEEN, Kansas City, Mo.

Hygiene; Growth and Nutrition; Public Health

PATTERN OF GROWTH. JOHN CAREY, Illinois M. J. **87**:33 (Jan.) 1945.

Clinically, physical and mental welfare are interdependent, and the boundary between the normal and the abnormal is not a fixed, but a shifting, standard. A survey of the factors involved in growth indicates the strategic position of pediatrists in the future scheme of medicine. Social factors have produced a growing demand for a periodic type of developmental supervision of the mental and physical progress. Recognition and correction of early deviation from normal will protect the potential capabilities of the child.

BARBOUR, Peoria, Ill.

Prematurity and Congenital Deformities

A CASE OF HEREDITARY MESIOCCLUSION COMPLICATED BY ENDOCRIN DYSFUNCTION. BROOKS BELL, Am. J. Orthodontics **29**:595 (Oct.) 1943.

Since striking anterior development of the mandibles of the patient's mother and maternal grandmother was noticed, a thorough physical examination was requested at the time treatment was suggested. The endocrinologist reported no endocrine disturbance.

Orthodontic treatment of class III, complicated by missing upper laterals, second premolars and left second permanent molar, was started at the age of 4, and continued for six years. At the age of 10 a different endocrinologist was consulted and his report showed a mild thyroid and pituitary deficiency.

As soon as the primary effect of the endocrine medication now being administered has passed, orthodontic treatment will be reinstituted. The author is pessimistic over the orthodontic results so far and the future outcome of the case.

LEWIS, Dayton. [ANGLE ORTHODONTIST]

Prematurity and Congenital Deformities

CRANIAL ANOMALIES. HERMAN JOSEPHY, Illinois M. J. **87**:39 (Jan.) 1945.

An outline of classification which has to serve as a basis for statistics and for a brief denomination of actual cases must be simple; it cannot enumerate every disease and abnormal condition. The classification is for clinical, and not for pathologic use. Many diagnoses which can be made at autopsy cannot be made by examination of the living patient.

Even a simplified outline should use as a basis for classification essential symptoms which point to something more than a superficial similarity. The conditions which are connected with cranial anomalies are too diversified to be grouped under a common heading. Therefore the term "developmental cranial anomalies" should disappear and should be replaced by more appropriate denominations, even at the risk of adding items to the classification of mental deficiencies.

BARBOUR, Peoria, Ill.

Newborn

A REVIEW OF OLD AND MODERN TREATMENT OF ASPHYXIA NEONATORUM. ISAAC A. ABT, Illinois M. J. **87**:19 (Jan.) 1945.

A historical review of the evolution of the treatment of asphyxia neonatorum is presented.

BARBOUR, Peoria, Ill.

THE VALUE OF SERUM PROTEIN DETERMINATIONS IN CASES OF SUSPECT ERYTHRODERMIA DESQUAMATIVA OF THE NEWBORN. KURT GLASER and SIMPSON MARKSON, J. Pediat. **26**:367 (April) 1945.

Conditions labeled "infantile eczema" may not always be harmless but may be the precursor of erythroderma desquamativum. This statement holds especially for conditions which do not undergo the usual remissions but show continuous progression (Hill reported 80 cases of eczema, with 21 cases of erythroderma). The type of diet does not seem to influence the condition to any significant degree; however, the utmost care has to be taken in selecting the diet to insure its adequacy. Special diets, "allergic," "elimination," "low fat" or "high protein" diets, have to be calculated as to their caloric values and constituents in order to avoid starvation effects and consequent tendency to hepatic injury. From this study it can be concluded that every case of so-called infantile eczema of prolonged duration and without the usual regressions should be considered potential erythroderma desquamativum, and the serum protein level should be determined. This determination will not only help in the prognosis but will indicate early treatment to replenish the blood stream, and thus the hepatic cells, with the necessary protein, before a severe parenchymatous injury to the liver occurs. Local treatment of the skin seems of little or no value.

FROM THE AUTHORS' SUMMARY.

Acute Contagious Diseases

TREATMENT OF SCARLET FEVER. MAX J. FOX and N. F. GORDON, Arch. Int. Med. **74**:1 (July) 1944.

Fox and Gordon review the therapeutic results in scarlet fever in two series of 1,000 cases each. They conclude that sulfonamide compounds find their chief value in the treatment of certain complications but are of no value in the management of the toxic phase of type of scarlet fever. The use of commercial antitoxin combats the toxic phase of the disease but introduces the danger of foreign protein reactions. Pooled human convalescent serum produced rapid clinical response when administered to patients with scarlet fever and offers the best means of therapy.

LYNCH, St. Paul. [ARCH. DERMAT. & SYPH.]

MYELITIS COMPLICATING MEASLES. LAURENCE A. SENSEMAN, Arch. Neurol. & Psychiat. **53**:3 (April) 1945.

A case of myelitis complicating measles in a man aged 24 is reported. The patient recovered completely without specific therapy.

BEVERLY, Oak Park, Ill.

VACCINIA OCCURRING AT SHORT INTERVALS. CARL A. MINNING, Bull. U. S. Army M. Dept., August 1944, no. 79, p. 82.

Seven hundred and seventeen officers and enlisted men were vaccinated by the multiple pressure method. All men were inoculated with cowpox virus of the same lot number. When the results of these vaccinations were recorded, it was found that vaccinia had been induced in 12 men who had experienced the same condition from ten to fifteen months previously. These men in all probability acquired only transient immunity to smallpox through the first attack of vaccinia. The author therefore concluded that if the spread of smallpox is to be prevented, in addition to periodic vaccinations, there

hould be routine inoculation with cowpox virus of all ersons exposed directly or indirectly, irrespective of he recency or of the results of previous vaccinations.

STRAKOSCH, Denver. [ARCH. DERMAT. & SYPH.

NDEMIC TYPHUS FEVER IN SOUTHERN CALIFORNIA. HENRY E. MELENEY and RALPH S. FRENCH, California & West. Med. **62**:119 (March) 1945.

An analysis is presented of the occurrence of endemic yphus in California. The disease to date has occurred lmost entirely in the southern portion of the state, he chief endemic areas being Los Angeles and San iego Counties, particularly the cities of Los Angeles nd San Diego.

The locally acquired disease is the murine type and as probably been so almost, if not entirely, since 1922. his is indicated by the sudden disappearance of the isease in 1925, following the vigorous rat control ampaign in Los Angeles in connection with the epiemic of pneumonic plague. It is also indicated by the easonal, sex and occupational distribution of cases, the w fatality rate and the general absence of human lice n patients.

The recent occurrence of a large proportion of cases rural areas, particularly associated with hog ranches nd race tracks, suggests that the disease in rats is ecoming more prevalent in rural areas.

Although the incidence of human cases of murine yphus in California is not yet alarming, its increase recent years emphasizes the necessity for the conuation of vigorous rat control measures in the cities nd thickly populated rural areas of southern California, nd also in cities farther north, which may become ndemic foci in the future.

PRYOR, Palo Alto, Calif.

ENINGOCOCCIC CONJUNCTIVITIS. R. D. REID and L. H. BRONSTEIN, J. A. M. A. **124**:703 (March 11) 1944.

A child of 2 years had purulent conjunctivitis of the ght eye. A smear showed numerous intracellular and tracellular gram-negative diplococci. The condition the eye grew worse. General examination revealed thing of significance except for a temperature of 6 F. Cultures of material made by rubbing the fresh wab of exudate on the surface of a chocolate agar ate yielded an abundant growth of oxidase-positive, am-negative diplococci. The organisms were agglunated with antimeningococcus serum type I and failed agglutinate with antimeningococcus serum type II III or with antigonococcus serum. With sulfathiaole therapy and irrigations of the eye with a solution boric acid, there was no longer any purulent disharge on the third day, and the child was dismissed om the hospital.

The authors conclude that the diagnosis of meningoccic conjunctivitis should be suspected in cases in hich gram-negative intracellular diplococci are seen smears of pus and no obvious source of the infection discernible.

ZENTMAYER. [ARCH. OPHTH.]

STUDY OF THE AGGLUTININ RESPONSE IN PATIENTS WITH MENINGOCOCCIC MENINGITIS. HARRY F. DOWLING, RUTH L. MAYER, LEWIS K. SWEET and EDITH DUMOFF-STANLEY, J. Clin. Investigation **24**:160 (March) 1945.

A study of the rise and fall of agglutinin titers uring the course of meningococcic infection was made by testing 284 specimens of serum from 69 patients with meningococcic meningitis or meningococcemia. All patients received sulfadiazine or sulfamerazine, and 2 of them received penicillin. In testing for agglutinins, a centrifugation method was employed instead of the usual procedure of heating the test serum with the suspension of meningococci to 37.5 C., followed by refrigeration. Serum agglutinin titers ranged from zero to 1:1,024 and, when positive, were generally specific for the group of meningococci isolated from the spinal fluid of the patient. The median titer for patients with type I agglutinins rose to 1:128 for the period from the eleventh to the fifteenth day, inclusive, and fell to zero in the period between the twenty-fifth and the thirtieth day. The greater the number of organisms present in the initial specimen of spinal fluid, the higher the median agglutinin titer. The authors conclude that the centrifugation-agglutination test is a simple and efficient method for the diagnosis of meningococcic infections when organisms cannot be cultured from the body fluids.

GUEST, Cincinnati.

A LABORATORY TEST FOR DIAGNOSIS OF SMALLPOX. C. E. VAN ROOYEN and R. S. ILLINGWORTH, Brit. M. J. **2**:526 (Oct. 21) 1944.

The purpose of this paper is to describe a laboratory test which was of great help in establishing the early diagnosis of smallpox. The test consists simply in getting scrapings of early lesions of smallpox from the face, putting them on clean glass slides and staining them with the Paschen method. A description of the technic and the stain is contained in the article. The authors state that it is important to look at a positive and a negative smear just before examining the specimen, in order to refresh one's mind concerning the appearance of the elementary bodies characteristic of smallpox. These bodies were found in 96 per cent of 80 specimens examined. A negative result was obtained in smears from 3 patients with smallpox. In no instance was a positive smear reported for a patient who did not have smallpox. This film test is not applicable to the diagnosis of chickenpox because the elementary bodies of varicella are too small and too scanty and do not have an affinity for Paschen's stain. This test has been of great help in making the early diagnosis of smallpox and is much more valuable than either the complement fixation test or the flocculation test, as the last two require from seven to ten days after onset of the infection to give a positive result.

BIRDSONG, Charlottesville, Va.

SPORADIC MENINGOCOCCAEMIA AMONG ROYAL AUSTRALIAN NAVAL PERSONNEL. J. K. MADDOX, M. J. Australia **2**:349 (Sept. 30) 1944.

Maddox describes 3 cases of subacute and chronic meningococcemia. The clinical combination of (1) intermittent fever with neutrophilic leukocytosis, the characteristic rose pink macules with hemorrhagic centers becoming localized—especially about the malleoli—in crops accompanying febrile phases, (2) tender muscles or joints and (3) preservation of fair general condition and concentration of red cells constitutes a syndrome characteristic of meningococcemia.

GONCE, Madison, Wis.

A SUGGESTED NEW TREATMENT OF POLIOMYELITIS. B. F. SAMPSON, South African M. J. **18**:421 (Dec. 23) 1944.

Because of the great variation in neuronic resolution in cases of poliomyelitis, the author suggests that the

virus produces the degeneration not so much by a discrete attack on the cells as by the calling into play of some secondary factor, and that this secondary factor works in a zonal manner. The secondary factor may be anoxia. The favorable influence of neostigmine and of the Kenny treatment may be due to vasodilatation of vessels in the spinal cord. Consequently, as soon as paresis appears and for the next three or four days, the reversibility of the changes in the cells of the horn might be favorably influenced by an increased oxygen supply to these cells brought about by the use of neostigmine, nicotinic acid or nikethamide. Reduction in blood pressure could be combated by application of a large pad and binder to the abdomen. Furthermore, in the treatment of poliomyelitis the daily intravenous injection of dextrose may be of importance, in view of Lawrence's work, which shows that neurons cannot utilize oxygen unless they have an adequate supply of dextrose. Finally, because of the known susceptibility of the virus to oxidizing agents, there would seem to be some rationale for pushing the administration of oxygen by whatever means can be devised.

GONCE, Madison, Wis.

Acute Infectious Diseases

SEROPROPHYLAXIS IN EXPERIMENTAL RABIES. KARL HABEL, Pub. Health Rep. **60**:545 (May 18) 1945.

A method for the production and concentration of rabies immune rabbit serum is described. In experimental animals this gave better results than the vaccine. The effects of serum prophylaxis were apparent up to three days after infection, and the serum was more effective when given intramuscularly at the site of inoculation with the virus. When used against street virus infection, the results were better when combined with vaccine prophylaxis.

SANFORD, Chicago.

Chronic Infectious Diseases

PENICILLIN IN THE PREVENTION AND TREATMENT OF CONGENITAL SYPHILIS. J. W. LENTZ, NORMAN R. INGRAHAM JR., HERMAN BEERMAN and JOHN H. STOKES, J. A. M. A. **126**:408 (Oct. 14) 1944.

Fourteen pregnant women with early syphilis and 9 infants with congenital syphilis were treated with penicillin. For pregnant women a dose of 2,400,000 Oxford units given intramuscularly round the clock in approximately eight days is recommended. Therapeutic or placental shock may occur. It may be avoided by considerably reducing the dose for the first thirty-six to forty-eight hours of therapy.

Infants with congenital syphilis responded well to a dosage of approximately 18,000 units per pound (36,000 units per kilogram) of body weight. Grossly infected syphilitic infants, however, may be injured by the injudicious use of penicillin.

HENSCHEL, Denver. [ARCH. DERMAT. & SYPH.]

TUBERCLE BACILLURIA IN THE CHILD. W. T. MONRO, Edinburgh M. J. **51**:101 (Feb.) 1944.

The author clearly states that the term "tubercle bacilluria" is used only when tubercle bacilli are found in the urine but without symptoms which suggest tuberculous disease in the genitourinary tract.

Tubercle bacilluria is evidence of an early invasion, while ulcerocavernous lesions are late manifestations; there are no intermediate stages. In all cases of tubercle bacilluria there is a history of bed wetting; few pus cells are found, but seldom are acid-fast bacilli demonstrable. Many patients with bacilluria recover. In some instances healing lesions have been shown in the sections. It is necessary for all patients to be under prolonged observation. In the child the difficulty is in recognizing the mild spread of the disease when the evidence is slight. The author concludes that the pulmonary lesions, like the renal ulcerocavernous lesions, are adult focal manifestations of an infection acquired in childhood.

NEFF, Kansas City, Mo.

Diseases of Blood, Heart and Blood Vessels and Spleen

COARCTATION OF THE AORTA: CLINICAL AND ROENTGENOLOGIC ANALYSIS OF THIRTEEN CASES. LAWRENCE PERLMAN, Am. Heart J. **28**:24 (July) 1944.

The author encountered 13 instances of coarctation of the aorta in the course of routine physical examination for army service of a group of men between the ages of 18 and 35 years. The incidence was approximately 1 : 10,000.

It is pointed out that coarctation should be suspected in all cases of hypertension. The patient should then be examined for faint or absent pulsation of the femoral artery and for pulsation of the intercostal vessels. The significant roentgenologic observations are absence of the aortic knob, aortic dilatation, enlargement of the left ventricle and erosion of the ribs.

GIBSON, Chicago.

STUDIES OF BONE MARROW IN VITRO: II. THE EFFECT OF HEMOGLOBIN AND RED CELL STROMATA ON ENGRAFTED BONE MARROW. M. RACHMILEWITS and A. ROSIN, Am. J. M. Sc. **208**:193 (Aug.) 1944.

The authors' experiments indicate that there is a distinct difference in the response to hemoglobin and to red cell stroma of the bone marrow surviving in vitro. The addition of hemoglobin to the standard medium resulted in an increase in the number of mature cells. The effect of stroma, on the other hand, was characterized by an increased number of immature cells, mainly precursors of red cells, and by a reduction of mature white cells. Both components of the erythrocyte had a stimulating effect on the bone in vitro. The stimulation caused by hemoglobin was manifested mainly in the direction of maturation, while the effect of stroma was seen in the direction of multiplication—particularly of the erythroid elements—thus producing in vitro an erythroblastic bone marrow.

HENSKE, Omaha.

THE SIGNIFICANCE OF MARKED LEFT AXIS DEVIATION OF THE ELECTROCARDIOGRAM. JAMES M. FAULKNER and CHARLES N. DUNCAN, Am. J. M. Sc. **208**:2[illegible] (Aug.) 1944.

The finding of marked left axis deviation in an otherwise normal electrocardiogram is to be regarded as a normal variation which, though encountered with increasing frequency with advancing age, cannot be correlated with ventricular enlargement, coronary disease or myocardial disease.

AUTHORS' SUMMARY.

SINOPHIL LEUKEMIA: WITH REPORT OF A CASE. MARION FRIEDMAN, IRVING J. WOLMAN and HARLAN H. TYNER, Am. J. M. Sc. **208**:333 (Sept.) 1944.

A case of leukemia in an 11 year old Negro boy is esented. Clinically, there were weakness, emaciation, ronic cough, generalized enlargement of the lymph des of the head and neck, hepatomegaly, dependent ema, a leukocyte count up to 194,000 cells per cubic llimeter, an eosinophil count ranging from 80 to 90 cent with nearly all mature cells and a decrease in al proteins with inversion of the albumin-globulin io. Necropsy demonstrated increase of mature and mature eosinophils in the bone marrow, with infiltion into lymph nodes, pelvic fascia, muscles of the ghs and back, salivary glands, lungs, stomach, nasal cous membrane and other tissues. The spleen was slightly involved. This instance and 12 others found the literature on hematology seem to be best characized as manifestations of leukemic overgrowth of the sinophile blood cells, though admittedly the nosologic sis for this interpretation rests solely on morphologic idence.

HENSKE, Omaha.

PRESSANT EFFECTS OF HIGH CONCENTRATIONS OF INSPIRED OXYGEN ON ERYTHROCYTOGENESIS: OBSERVATIONS ON PATIENTS WITH SICKLE CELL ANEMIA WITH A DESCRIPTION OF THE OBSERVED TOXIC MANIFESTATIONS OF OXYGEN. E. H. REINHARD, CARL V. MOORE, REUBENIA DUBACH and LEO J. WADE, J. Clin. Investigation **23**:682 (Sept.) 1944.

During six periods of eight to twenty days each, 4 tients with sickle cell anemia breathed 70 to 100 per nt oxygen administered through a Boothby-Lovelace-lbulian mask. The observed effects were (1) a crease in the degree of intravascular sickling of red od cells and (2) depression of erythrocytogenesis. e latter effect was reflected in a decrease of both ticulocytes and red blood cells in the circulation. ter inhalation of oxygen was discontinued, a striking ticulocytosis developed, and the red cell count returned the preoxygen level. It is suggested that the dession of erythrocytogenesis by increased oxygen sion following administration of oxygen is the ysiologic antithesis of the stimulation of red cell rmation produced by low oxygen tensions. Only nor toxic manifestations developed during the periods oxygen therapy.

GUEST, Cincinnati.

HE NUTRITIVE VALUE OF HUMAN PLASMA FOR THE RAT. D. M. HEGSTED, J. M. MCKIBBIN and F. J. STARE, J. Clin. Investigation **23**:705 (Sept.) 1944.

Human plasma proteins are inadequate as the sole urce of protein for the growing rat. A low content isoleucine is the primary amino acid deficiency. A pplement of 0.5 per cent d,l-isoleucine gives a near ximum response.

FROM THE AUTHORS' SUMMARY.

RUM ALBUMIN REGENERATION AS EFFECTED BY INTRAVENOUSLY AND ORALLY ADMINISTERED PROTEIN HYDROLYSATES. WARREN M. COX JR. and ARTHUR J. MUELLER, J. Clin. Investigation **23**:875 (Nov.) 1944.

Enzymic hydrolysates of casein, lactalbumin and beef rum protein, nutritively equivalent to the original oteins, were found to be equally effective in the reneration of plasma albumin in hypoproteinemic dogs, whether given orally or intravenously. The authors discuss the significance of these observations in relation to previously recorded differences in the ability of these proteins, when fed intact, to regenerate plasma albumin. It is not unlikely that differences in the rate of protein hydrolysis and in the rate of absorption of the amino acids from the intestinal tract may greatly influence the effectiveness of a particular protein in regeneration of serum albumin. The authors point out that in measuring the effect of an ingested protein by means of plasma albumin regeneration one may be measuring not an intrinsic difference in the proteins but the net result of varying rates of enzymic hydrolysis and absorption from the intestine.

GUEST, Cincinnati.

AUTOHEMAGGLUTININS — "COLD AGGLUTININS." CUTTING B. FAVOUR, J. Clin. Investigation **23**:891 (Nov.) 1944.

A broad study of the occurrence of cold agglutinins in normal subjects, in persons with infections of the respiratory tract and in a number of general hospital patients was undertaken as a part of a general investigation on the relation between atypical pneumonias and the common infections of the respiratory tract. The report extends the list of conditions associated with the presence of cold agglutinins, indicating that the agglutinins may be associated with a variety of noxious stimuli. While a titer of 1:40 was found with a variety of diseases, a titer of 1:160 was uncommon except with severe atypical pneumonia. Eighteen of 46 patients with atypical pneumonia had a serum agglutinin titer of 1:160 or higher. The agglutinins may persist after atypical pneumonia for nine months or may appear and disappear without evident infection. The cold agglutinin test was regarded as useful in clinical diagnosis when the results are carefully interpreted with other observations.

GUEST, Cincinnati.

THE INFLUENCE OF "HEART STIMULANTS" ON THE CONTRACTION OF ISOLATED MAMMALIAN CARDIAC MUSCLE. STEPHEN KROP, J. Pharmacol. & Exper. Therap. **82**:48 (Sept.) 1944.

Because of the great differences of opinion concerning the true action of the so-called heart stimulants, this study was undertaken. To eliminate all contributory side actions, experiments were made on segments of papillary muscles from the right side of the heart of the cat. The conclusions, which seemingly were clearcut, are as follows, but the original article should be read for a discussion of the results: Camphor, metrazol, nikethamide and barium chloride had no digitalis-like action.

The xanthines (caffeine, theobromine and theophylline) are ineffectual except in concentrations considerably above those attainable therapeutically. Compared with digitalis glucosides, their action is rapid in onset and brief in duration.

Epinephrine augments the "systolic" force of mammalian heart muscle to a pronounced degree and in concentrations attainable with therapeutic doses. The effect is almost immediate in onset; its duration is a matter of only about ten to twenty minutes rather than the hours of duration of the digitalis glucosides. As could be expected, epinephrine had a decided action and in therapeutic concentrations. Ephedrine also in "therapeutic" doses was a stimulant, but the range between the concentration which stimulates and that which depresses the heart muscle is small. The author agrees

with others who have studied the drug that the stimulant action of ephedrine is probably due to its epinephrine content.

PILCHER, Cleveland.

CONGENITAL HEART LESION: PULMONARY STENOSIS AND INTRAVENTRICULAR SEPTAL DEFECT: REPORT OF A CASE. MAURICE HARDGROVE and ANTHONY GRAMLING, Wisconsin M. J. **43**:793 (Aug.) 1944.

A 6 year old boy for whom a diagnosis of congenital heart disease was made died suddenly with edema, cyanosis and dyspnea after seven months of an apparently mild infection of the respiratory tract without fever. Autopsy revealed septal patency, an enlarged right ventricle and an underdeveloped pulmonary artery. There were vegetations of active endocarditis and an old thickening of the valves, indicating that the child had had a superimposed rheumatic endocarditis with a recent acute endocarditis causing death.

BAIRD, Wauwatosa, Wis.

ANGIOCARDIOGRAPHY IN CHILDREN: ITS DIAGNOSTIC VALUE. R. KREUTZER, J. M. PELLIZA and S. CALISTI, Arch. argent. de pediat. **22**:32 (July) 1944.

The procedure of angiocardiography as developed by Castellanos and others is described. The dosage of radiopaque substance is related to age, weight and degree of cyanosis. No by-effects have been reported, solutions up to 50 per cent being used. Vasomotor reactions, apnea, nausea and other reactions have been reported with the use of 75 per cent solutions of diodrast. Adequate timing of the roentgenograms is necessary to achieve the best results. The authors describe 2 clinical cases in which the diagnosis was made with this procedure.

CASSORLA, Chicago.

Diseases of Nose, Throat and Ear

ROENTGENOGRAPHIC DIAGNOSIS OF COMPLICATIONS OF MASTOIDITIS. PEDRO REGULES and NICOLAS CAUBARRERE, An. de oto-rino-laring. d. Uruguay **14**:21, 1944.

The authors attempt to establish criteria for diagnosing the complications of mastoiditis. Their article deals primarily with interpretations of the roentgenographic findings, particularly those in the region of the lateral sinus. They describe what they term the gutter, which runs anteriorly along the entire course of the sinus wall, and in the interpretation of the defects they believe that an alteration of the anterior wall of the gutter of the sinus is a positive sign of pathologic involvement of the sinus. In a group of 24 cases they were able to diagnose sinus disease preoperatively in 19 cases. The importance of this criterion is evident particularly when the symptoms are more or less latent, when the mastoiditis may be due to Pneumococcus mucosus or when treatment with sulfonamide compounds has been instituted and many of the findings are masked. In such cases prognosis is always graver and the need for surgical intervention more urgent.

PERSKY, Philadelphia. [ARCH. OTOLARYNG.]

ETIOLOGY AND PATHOLOGY OF THE DEFORMITIES OF THE NASAL PYRAMID. ALFREDO ALCAINO, Rev. de otorhinolaring. **3**:184 (Dec.) 1943.

Alcaino discusses nasal deformities from the physiologic and esthetic standpoints. He stresses the fact that nasal reconstruction should be done by the rhi ologist.

He divides the nasal pyramid into two parts: t osseous, which constitutes the vertex, and the car laginous, which forms the base. The nasal septum also divided into two parts: a posterior bony portio which articulates with the bony vertex, and an anteri cartilaginous portion, which articulates with the car laginous base. Thus the nasal skeleton is divided in a fixed posterior portion and a movable anterior portio The author believes that alterations in the developme of the superior maxilla and of the palatine arches a responsible for many of the nasal deformities. The processes form the nasal floor and the hard pala Their deformity produces a high palate with shortenin of the vertical nasal diameter, which in turn preven full development of the nasal septum, and this produc septal deviations.

Nasal deformities are: 1. External deformitie rhinomegalia, hump nose, lateral deviation, and hype trophy of the nasal tip. 2. Internal deformities: septa deviations altering the normal respiration, also narro noses which do not permit proper ventilation. Deformities of the base; congenital or traumatic de formities of the columella. He also mentions the shor upper lip, which may cause an esthetic deformity whe the patient tries to close his month and thus pull down the tip of his nose.

PERSKY, Philadelphia. [ARCH. OTOLARYNG.

Diseases of Lungs, Pleura and Mediastinum

THE INFLUENCE OF B VITAMINS ON THE RESISTANC OF RATS TO INDUCED PNEUMOCOCCAL LOBAR PNEU MONIA. HARRY J. ROBINSON and HENRY SIEGE J. Infect. Dis. **75**:127 (Sept.-Oct.) 1944.

1. Rats deficient in riboflavin or in pantothenic ac are as resistant to experimentally induced pneumococc lobar pneumonia as rats receiving the same basal di supplemented with adequate quantities of riboflavin pantothenic acid.

2. Deficiency of thiamine and possibly of pyridoxi appeared to lower the resistance of rats to this infec tion somewhat below that of the group receiving th same basal diet plus all the B vitamins.

3. With the exception of rats having thiamine defi ciency all deficient groups, including those on a com plete synthetic diet deficient in unknown factors, showe a greater resistance to infection than rats fed the nor mal stock diet ad libitum.

4. Inanition had no apparent influence on the resi tance of rats.

5. There was essentially no difference in the rate degree of growth of pneumococci, added to the bloo of deficient and of healthy rats.

TOOMEY, Cleveland.

INTRATHORACIC CYST OF GASTRIC TYPE: ONE-STAG REMOVAL. R. S. PILCHER, Proc. Roy. Soc. Me **37**:576 (Aug.) 1944.

The patient, aged 1 year, was admitted to the hos pital in September 1941, with a history of swellin of the abdomen and unsatisfactory progress for fiv months On examination the child was found to hav a large space-occupying lesion in the right side of th chest. The swelling of the abdomen appeared to b due to downward displacement of the liver. In Octo ber the cyst was removed and was seen to have it main attachment and blood supply in the upper par of the paravertebral gutter, where, no doubt, the sym

athetic nerve fibers were damaged, as the child after peration had Horner's syndrome and a dry upper yelid. The lung, which presumably had been col-psed for some months, rapidly expanded.

WILLIAMSON, New Orleans.

RONCHOPNEUMONIA IN PREMATURE TWINS. H. NOTTI, Arch. argent. de pediat. **22**:516 (Dec.) 1944.

Penicillin was used in the treatment of premature wins having bronchopneumonia at the age of 7 weeks. he author considers penicillin to have been the prin-pal factor in their recovery. Administration of oxy-en, transfusion of blood and use of sulfonamide mpounds were the other therapeutic means employed. o roentgenologic examination was made, and the usal organism was not identified. No by-effects ere observed after the administration of penicillin.

CASSORLA, Chicago.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

ALMONELLA ENTEROCOLITIS IN INFANTS AND CHIL-DREN. ERWIN R. NETER and PHYLLIS CLARK, Am. J. Digest. Dis. **11**:323 (Oct.) 1944.

This is the report of a study of 21 bacteriologically roved cases of enterocolitis due to Salmonella en-untered at the Children's Hospital, Buffalo, in 1943. he ages of the patients ranged from 11 days to 12 ears; 10 were less than 3 months and 18 less than years of age.

Some of the patients became infected while being eated in the hospital for other conditions. There were deaths. One of the patients who died was among the 4 treated with sulfonamide compounds. In 11 of the atients the disease was due to Salmonella typhi urium and in 1 to the unusual Salmonella Thompson rganism.

LESLIE, Evanston, Ill.

EPATITIS DUE TO THE INJECTION OF HOMOLOGOUS BLOOD PRODUCTS IN HUMAN VOLUNTEERS. JOHN R. NEEFE, JOSEPH STOKES JR., JOHN G. REINHOLD and F. D. W. LUKENS, J. Clin. Investigation **23**:836 (Sept.) 1944.

The fact that human plasma or serum may contain a ansmissible agent capable of producing hepatitis has en confirmed by the results of the inoculation of 9 uman volunteers. Hepatitis occurred with and with-ut jaundice and in some cases would not have been tected if studies of hepatic function had not been rried out at frequent intervals. Six of the 9 patients d the onset of the disease from twelve to thirty-five ys after inoculation. One volunteer who was re-oculated with the same material after recovery from e first attack showed no evidence of hepatitis during ne hundred and forty days of subsequent observation. wo cases of jaundice may have occurred as a result contact with one of the volunteers. Observations uggesting the generalized nature of this disease are und in the report of a case in which ileitis and esenteric adenitis were observed at laparotomy.

GUEST, Cincinnati.
[FROM THE AUTHORS' SUMMARY]

STATISTICAL SURVEY OF APPENDICITIS IN CHILDREN. S. G. ANDERSON, M. J. Australia **2**:567 (Nov. 25) 1944.

The author analyzed the records of 923 cases of ppendicitis in children with respect to symptoms, posi-tion of appendix, convalescence, wound infection and mortality rate. In 38 of a total of 45 cases of children under 3 years of age, the sequence of symptoms as given explicitly by the parents was recorded as follows: pain followed by vomiting, 9 cases; vomiting followed by pain, 25 cases; pain and vomiting simultaneously, 4 cases. This preponderance of cases in which, according to the parents, vomiting was the first symptom or sign, did not appear in the cases of children over 3 years of age.

GONCE, Madison, Wis.

STUDIES OF THE ACUTE DIARRHEAL DISEASES: XIV. CLINICAL OBSERVATIONS. ALBERT V. HARDY, Pub. Health Rep. **60**:521 (May 11) 1945.

In a series of 1,247 cases of acute diarrheal disease, positive cultures for Shigella paradysenteriae were obtained in 555 cases. The symptoms in the groups were approximately the same. In fact, "simple diarrhea" rather than classic dysentery was the usual manifestation of infection with S. paradysenteriae.

SANFORD, Chicago.

CHYLOTHORAX AND CHYLOPERITONEUM IN AN INFANT. F. SCHWEIZER, J. A. TRAVERSARO and T. M. BANZAS, Arch. argent. de pediat. **22**:300 (Oct.) 1944.

A case of chyloperitoneum and chylothorax in a 40 day old infant is reported. The onset was sudden, with intense dyspnea and cyanosis. Physical signs of pleural effusion were observed, and a milky fluid was obtained by pleural tap. There were, in addition, signs of accumulation of fluid in the peritoneal cavity and a voluminous inguinoscrotal hernia on the right side. The hernial sac was tapped, and a similar fluid was obtained. The physical and chemical characteristics of these fluids were those of chyle. Subsequently, several taps were made to relieve the severe dyspnea; the fluid obtained had the same characteristics as those previously obtained. The child was discharged at the request of the family.

The presence of a congenital anomaly of the chyle ducts is assumed by the authors to interpret and explain adequately the clinical picture shown by this infant.

The literature dealing with this subject is reviewed.

CASSORLA, Chicago.

ACUTE APPENDICITIS IN INFANTS. J. DAMIANOVICH and A. VIDAL FREYRE, Arch. argent. de pediat. **22**: 383 (Nov.) 1944.

The authors report 14 cases of acute appendicitis in infants. All the diagnoses were confirmed at operation and by histopathologic studies of the appendix.

The national and the foreign literature are reviewed. The simultaneous occurrence of infection of the upper respiratory tract and appendicitis, so often observed, should be considered not as a coincidence but as an association of conditions commonly seen in infants.

The high mortality rate reported by several authors would tend to decrease if diagnosis were made early and surgical intervention performed.

The following conclusions are drawn: 1. Acute appendicitis in infants is more frequent than is commonly believed. 2. Abdominal pain in infants should always be carefully considered, and the possibility of acute appendicitis should be borne in mind. 3. All patients operated on by the authors before perforation occurred have recovered.

CASSORLA, Chicago.

ATRESIA OF THE ESOPHAGUS. E. G. CASELLI, Arch. argent. de pediat. **22**:426 (Nov.) 1944.

The case of a 5 day old infant with atresia of the esophagus is reported. Clinical diagnosis was confirmed by roentgenologic examination and by catheterization. At operation a tracheoesophageal fistula was found. The infant died a few hours after the intervention.

The author describes the different varieties of tracheoesophageal fistula.

CASSORLA, Chicago.

Nervous Diseases

THE CHEMOTHERAPY OF INTRACRANIAL INFECTIONS: IV. THE TREATMENT OF PNEUMOCOCCAL MENINGITIS BY INTRATHECAL ADMINISTRATION OF PENICILLIN. COBB PILCHER and WILLAM F. MEACHAM, J. Neurosurg. **1**:76 (Jan.) 1944.

Meningitis was produced in several groups of 10 to 14 dogs each by injection of type I pneumococci into the cisterna magna. Half of each group of animals were treated with penicillin, and the remaining half were used as controls. A total of 96 experiments were performed.

In the first series (48 experiments) 50 units of penicillin was injected intrathecally daily with slight but definite improvement as compared with the condition of the untreated controls. In the second series, of two groups of 12 dogs each, doses of 100 and 200 units of penicillin respectively were injected intrathecally daily; almost half the treated animals survived, and most of the deaths were due to lobar pneumonia. Because of the resulting pneumonia, a third series (24 dogs) were treated with the intrathecal injection of 200 units of penicillin daily and the intravenous injection of 1,000 units three times daily; the results were even more favorable than those in the second series.

WHITELEY, Philadelphia.
[ARCH. NEUROL. & PSYCHIAT.]

Diseases of the Ductless Glands; Endocrinology

CONCERNING THE HYPERSENSITIVITY OF ADRENALECTOMIZED RATS TO VASCULAR STRESS. OSCAR HECHTER, Endocrinology **36**:77 (Feb.) 1945.

Although it is well established that the adrenalectomized animal is hypersensitive to vascular stress, the compensatory mechanisms which fail in the absence of adrenocortical hormones have not been directly demonstrated. The present work was undertaken to determine whether the hypersensitivity of adrenalectomized animals could be due to a primary failure of compensatory mechanisms for maintenance of venous return and cardiac output.

It appears likely that the failure of a venopressor mechanism suggested by these studies participates qualitatively in the development of hypersensitivity following adrenalectomy in situations of vascular stress.

JACOBSEN, Buffalo.

INFLUENCE OF THIOUREA ON PLASMA PROTEINS AND ORGAN WEIGHTS IN THE RAT. JAMES H. LEATHEM, Endocrinology **36**:98 (Feb.) 1945.

A rise in total plasma protein concentration occurred in male rats fed 1 per cent thiourea for twenty to twenty-two days. This increase in total protein was due entirely to an increase in plasma globulin, sin the concentration of plasma albumin did not chang Thus the changes in blood protein simulated those o served after thyroidectomy.

Assay of the pituitary for gonadotropic hormone re vealed a greater hormone content in the glands thiourea-fed rats.

JACOBSEN, Buffalo.

THE CAUSE OF ABNORMAL RETENTION OF INGEST WATER IN ADRENALECTOMIZED RATS. REGINALD SHIPLEY, Endocrinology **36**:118 (Feb.) 1945.

It is well recognized that there is a failure of norm diuresis after the ingestion of large amounts of wat in adrenalectomized animals, as well as in patients wi Addison's disease, and the water test has become we established as a useful laboratory adjunct in the diag nosis of the latter condition.

The mechanism of the failure of diuresis in th presence of adrenal insufficiency has not been exte sively studied.

The experiments here reported were designed t find where in the body the ingested water is held. was found that although there is a demonstrable dela in the intestinal absorption of water in adrenalectomize rats and a decreased emptying time of the stomac these are only minor causes of failure of excretion wh water is ingested in large quantities. The greate portion of the administered water is retained in th extracellular compartment and probably remains u excreted because of failure of elimination by the kidn

JACOBSEN, Buffalo.

THE EFFECTS OF BILATERAL CERVICAL SYMPATHECTO ON THYROID ACTIVITY. GEORGE H. LOWE JR., A. Ivy and SAM BROCK, Endocrinology **36**:130 (Feb 1945.

This investigation was undertaken to obtain furth evidence regarding the functional innervation of t thyroid gland. The authors were primarily interest in ascertaining whether bilateral cervical sympathe tomy in guinea pigs altered the metabolic response a preparation containing the thyrotropic principle of t anterior lobe of the pituitary and to exposure to col

The results of the experiments are interpreted indicating that the cervical sympathetic nerves inhib perhaps by vasoconstrictor activity, either the produ tion of thyrotropic hormone or the output of thyro secretion.

JACOBSEN, Buffalo.

HYPOPHYSEAL STIMULATION BY INJECTION OF LIGH INACTIVATED ESTRONE. FRANK H. J. FIGGE, End crinology **36**:178 (Feb.) 1945.

Experiments on rats using estrone inactivated l light indicate that inactive degradation products estrogens stimulate the production and release gonadotropic factors from the anterior lobe of t pituitary.

JACOBSEN, Buffalo.

THE EFFECT OF LIMITED WATER INTAKE ON BO WEIGHT AND THYROID WEIGHT OF RATS TREAT WITH THIOURACIL. CHARLES M. WALDO and E WARD W. DEMPSEY, Endocrinology **36**:286 (Apri 1945.

Rats receiving thiouracil were partially protecte against loss of weight resulting from a restricted wat

intake. There was no evidence that the output of pyrotropic hormone was reduced in response to the restricted water intake. JACOBSEN, Buffalo.

THE EFFECTS OF TESTOSTERONE AND TESTOSTERONE PROPIONATE ON RENAL FUNCTIONS IN MAN. CALVIN KLOPP, NELSON F. YOUNG and HOWARD C. TAYLOR JR., J. Clin. Investigation **24**:189 (March) 1945.

The administration of testosterone or testosterone propionate in amounts presumed to be adequate for renotropic effects did not alter significantly the rate of glomerular filtration, the renal flow, the maximum rate of tubular secretion of para-aminohippurate or the maximum rate of tubular reabsorption of dextrose in normal subjects and in 5 patients with impaired renal function. GUEST, Cincinnati.
[FROM THE AUTHORS' SUMMARY]

Diseases of the Eye

PNEUMO-ENCEPHALOCELE, SECONDARY TO A PUNCTURE WOUND OF THE LID. H. SLAUGHTER and B. Y. ALVIS, Am. J. Ophth. **27**:617 (June) 1944.

The case of a child who presumably injured her lid with a pencil is described. Pus was obtained when the lid was incised, culture of which showed Staphylococcus aureus. A diagnosis of traumatic pneumoencephalocele was made on the basis of the roentgenogram. The child recovered. W. S. REESE. [ARCH. OPHTH.]

A REPORT ON A FAMILY WITH ECTOPIC LENSES. C. A. CLAPP, Am. J. Ophth. **27**:738 (July) 1944.

Clapp reports on 11 children in one family, of whom 4 have misplaced lenses and a ninth has congenital cataract. W. S. REESE. [ARCH. OPHTH.]

CONGENITAL DEFICIENCY OF ABDUCTION OF THE EYES. (DUANE'S SYNDROME). A. J. ELLIOT, J. Canad. M. Serv. **1**:437, 1944.

Elliot reports 3 cases of congenital deficiency in abduction of the eyes. In 1 case a bilateral retraction syndrome was present, while in the other 2 cases a unilateral retraction syndrome was found. A limited review of the literature is given.

The article is illustrated.

ZENTMAYER. [ARCH. OPHTH.]

CONGENITAL FOLDS OF THE RETINA. A. VAZQUEZ BARRIERE and L. A. BOADO, Arch. de oftal. de Buenos Aires **18**:572 (Nov.) 1943.

This malformation consists in a crease of the retina, forming a fold above the retinal plane, always beginning at the papilla and spreading toward the periphery in fan fashion. Frequently the peripheral end extends beyond the limits of the ophthalmoscopic field, reaching the ciliary body and even the equator of the crystalline lens.

Only four important papers on this condition have appeared thus far, and up to the time of writing only 40 cases have been reported in the literature.

The authors describe 2 cases illustrating this rare condition. H. F. CARRASQUILLO. [ARCH. OPHTH.]

Skin Diseases; Allergy

STATUS OF POISON IVY EXTRACTS: REPORT OF THE COUNCIL ON PHARMACY AND CHEMISTRY. FRANKLIN A. STEVENS, J. A. M. A. **127**:912 (April 7) 1945.

Present chemical and biologic evidence suggests that the same active agent is present in the saps of poison ivy, oak, sumac and lac plants and, therefore, that a single extract may be used in the treatment of the dermatitis they produce. The active agent, urushiol, a mixture of oils is readily oxidized and inactivated by the enzyme laccase, which is activated as soon as the sap is exposed to air. Ether extracts containing urushiol but little enzyme are probably most satisfactory for clinical use.

All the evidence indicates that dermatitis occurs only after sensitization. Protection against dermatitis is obtained by desensitization not by immunization, and hence may be of short duration. Cutaneous tests are a measure of the sensitivity of the subject on rigorous exposure. Protection may be obtained by oral ingestion of ivy extracts, the amount of gastrointestinal reaction being related to the dose. This method can change positive cutaneous reactions but is still in the experimental stage. Although there is no evidence that sensitivity as measured by cutaneous tests has been modified by intramuscular injections, the reported clinical success with subjects who had experienced casual exposure has made this method at present the one of choice. Unfortunately, there is no accepted method of standardization of extracts.

"The treatment of the acute rash with ivy extracts should be discouraged." BAIRD, Wauwatosa, Wis..

Surgery and Orthopedics

PLASMA, GELATIN, AND SALINE THERAPY IN EXPERIMENTAL WOUND SHOCK. W. W. SPRINGLE and W. KLEINBERG, Am. J. Physiol. **141**:713 (July) 1944.

Administering small infusions of plasma, gelatin and saline solution intermittently over a period of hours apparently is a more effective method of preventing shock than giving a single massive infusion immediately after an injury occurs. NOURSE, Cleveland.

Society Transactions

CHICAGO PEDIATRIC SOCIETY

MORLEY D. MCNEAL, M.D., *President, in the Chair*

Dec. 19, 1944

Mortality Trends in the Newborn. DR. A. H. PARMELEE.

A study of infant mortality based on the data released by the United States Bureau of the Census for the year 1940 reveals that the mortality rate for the first year of life was 47 per thousand live births; the rate in 1930 was 64.6. This is a reduction of 12.4 per thousand live births as compared with the number for 1930. The data also show that in 1940 the mortality rate for the first month, which may be called the neonatal period, was 28.8 per thousand, and in 1930 was 35.7, or a reduction of about 6 per thousand. This is a creditable record of progress, but it still means that 61 per cent of all deaths in the first year of life occurred during the first month. In the United States, 67,886 babies of 2,360,399 born alive in 1940 died during the first month; 54,979 of these, or 83.3 per cent, died during the first week of life. Even more important in this discussion is the fact that 32,870, or 50 per cent, of all the deaths of the first month were in the first day of life.

When the figures for 1940 are compared with those for 1930, the mortality for the first day is found to be 13.9 per thousand in 1940, 15 per thousand in 1930 and also 15 per thousand in 1915; in the last twenty-five years there has been an improvement of only 1 more baby saved out of each thousand. Prenatal and natal causes were responsible for 84 per cent of the deaths during the first month in 1940, of which 46 per cent were due to premature birth, 15 per cent to injury at birth, 11 per cent to congenital malformations and 12 per cent to other prenatal and natal causes. Causes of death in the neonatal period, corroborated by necropsy, of 483 infants (Potter and Adair) were: birth trauma, 41.2 per cent; major anomaly, 14.5 per cent; suffocation and aspiration, 17.2 per cent; prematurity, 9.1 per cent; pneumonia and infections, 5.8 per cent, and syphilis, 2.9 per cent. Causes of death, demonstrated at necropsy, of 1,043 infants less than 14 days of age (Bundesen) were: intracranial hemorrhage, 22.7 per cent; malformations, 15.6 per cent; infections, 9.8 per cent; asphyxia, 6.2 per cent and prematurity, 30 per cent. These facts make it quite obvious that reduction of neonatal mortality is largely the responsibility of the obstetrician.

The responsibility, however, is a joint one. A knowledge of the anatomic, physiologic and chemical peculiarities of the newborn is essential to an adequate understanding of neonatal problems and indispensable to their proper care. There has been a definite improvement in the nursery care of the newborn due to pediatricians, and a new interest in the problems of the newborn has resulted in study and research which has added greatly to the knowledge in this important field. Obstetricians have benefited by this increased knowledge. Through these joint efforts and with the help of physiologists and pathologists, a great deal has been learned about the physiology of the fetus; for example, about the influence of the health and nutrition of the mother on the fetus and about the importance of prolonging intrauterine life as long as the safety of the mother will permit, in order to increase the viability of the prematurely born infant. A clearer understanding has been gained of the hazards of adjustment to extra-uterine life. This realization of the joint responsibility of pediatricians and obstetricians toward neonatal problems is, in my opinion, the most encouraging advance yet made in this field. Potter and Adair have stated that the major causes of death which may at least in part yield to attack are prematurity, birth injury, anoxemia, infections and exposure to unfavorable conditions of external environment immediately after birth.

Maternal health is recognized as a factor in neonatal morbidity and mortality. Any disease of the mother, whether it is infectious or metabolic, acute or chronic, may affect the fetus or contribute to the difficulties of birth and add to the difficulties of the newborn infant's adjustments. Of particular interest are toxemia of pregnancy, heart disease, nephritis, tuberculosis, malignant growth, disturbance of the thyroid gland, diabetes, syphilis and nutritional disturbance, both quantitative and qualitative. Vitamin deficiencies are receiving much attention now, lack of vitamin K, also of thiamine (vitamin B_1) and ascorbic acid (vitamin C). The influence of maternal health on neonatal mortality is illustrated by the following statistics from the Cook County Hospital for the years 1932, 1933 and 1934: total births, 13,543; stillbirths, 521 (3.84 per cent) and infant deaths, 418 (3.1 per cent). Of these, there were in ward 5 (normal obstetric cases): total births, 8,897; stillbirths, 108 (1.2 per cent) and infant deaths, 79 (0.9 per cent).

In ward 50 (pathologic obstetric and afebrile medical cases) there were: total births, 2,557; stillbirths, 25 (9.9 per cent) and infant deaths, 195, or 7.6 per cent. In ward 43 (septic, infectious and venereal cases) there were: total births, 2,089; stillbirths, 160 (7.7 per cent) and infant deaths, 144 (6.9 per cent). This means that 81 per cent of all the infant deaths and 80 per cent of the stillbirths occurred among 34 per cent of the mothers and that they were the mothers who were sick or had obstetric pathologic conditions. This corresponds to results obtained from a study of the records of 9,3[illegible] consecutive live births at the Presbyterian Hospital. Of the infants of 6,007 mothers considered healthy, 5[illegible] per cent were premature and 1.8 per cent died. Of the infants of 3,358 mothers who had some medical complications, 8.4 per cent were premature and 3.5 per cent died.

One of the most significant practical contributions to the reduction of neonatal mortality has been the great improvement in the care of premature infants, for which pediatrics has been largely responsible.

The nursery for newly born infants, under the supervision of a pediatrician, seemed to many pediatricians a few years ago a long step toward the answer to the problems of the newborn. Where this was put into effect, there was a definite improvement in the care of the newborn, but not the drop in mortality expected by some. The optimism of some pediatricians obviously could not be held by those who had studied the problem carefully. It is plainly indicated by the facts set down in this paper that only by a careful cooperative effort of obstetricians and pediatricians can there be hope for a significant improvement.

Advances in knowledge of the problems of the newborn due to the cooperative efforts of the obstetrician and the pediatrician have been encouraging. There remains much that can be done by a more general recognition of their joint responsibility. Some of the ways by which the problems of the newborn can be made easier and future neonatal mortality statistics can be improved through cooperative effort are suggested herewith:

1. Better teaching of the physiology and pathology of the newborn to medical students, interns, residents and nurses.

2. More and better autopsies performed on infants dying during the newborn period and on stillborn infants.

3. Proper hospital organization for the control of the technic of the maternity division, including the maternity nursery.

4. A cooperative, self-perpetuating organization of the obstetric and pediatric interns, residents and nurses in the larger hospitals to take care of neonatal emergencies: a "lifesaving team" for the delivery room and the nursery.

Cold Agglutinins as a Cause of Hemolysis in Erythroblastosis Neonatorum. Dr. Heyworth N. Sanford and Dr. Jesse R. Gerstley.

A child having Rh-positive blood of group A_1 of a father with Rh-positive blood of group A_1 and a mother with Rh-negative blood of group A_1B had the classic symptoms of erythroblastosis fetalis. She was given transfusions from five group A_1 donors, of whom 4 had Rh-positive and 1 Rh-negative blood. There was no improvement in the condition, and an intense hemolysis occurred. It was then observed that the child's blood contained irregular isoagglutinins that clumped the donor's blood at 0 C. but did not clump the same cells at 20 C. or 37 C. in vitro. Recovery occurred at once when the child was given a transfusion of Rh-positive blood of group A_1 from two donors whose blood was not acted on by the child's cold agglutinins.

During this period of hemolysis the child had an icterus index of more than 450 for eleven days. This did not cause kernicterus or harm the child in any way. Attention is called to the fact that in transfusions this type of hemolytic reactions of the newborn may be due to this kind of irregular isoagglutinins, and donors should be changed frequently, even if group compatible, and that kernicterus is not a necessary sequel to the hemolysis of blood in these instances.

Diaphragmatic Paralysis in the Newborn. Dr. A. B. Schwartz.

The close proximity of the phrenic nerve to the brachial plexus should make it fairly vulnerable to injury during obstetric maneuvers involving stretching the neck muscles of the infant. The phrenic nerve is derived from the third, fourth and fifth cervical nerves; the part of the brachial plexus usually injured in Erb's palsy is that portion derived from the fifth and sixth cervical nerves. The apparent rarity of diaphragmatic paralysis may be due to the difficulty of recognition by physical examination.

The subject of this report was a 3 week old baby brought in because of an unexplained cough. Examination revealed irregularity in respiratory movement of the two sides, impaired resonance to percussion and suppression of breath sounds over the lower lobe of the left lung. A concomitant Erb's palsy suggested the diagnosis of paralysis of the phrenic nerve, a supposition which was confirmed by roentgenographic study. The baby exhibited the three classic signs which have been mentioned by previous observers as diagnostic of this condition: Duchenne's sign, a flattening of the epigastrium during inspiration in contrast to the normal ballooning; Hoover's sign, an increased expansion of the lower thoracic diameter during inspiration, and the spectacular Kienböck's sign, consisting of the paradoxic movement of the diaphragm when seen under the fluoroscope. During inspiration, as the sound side of the diaphragm descends the flaccid side ascends; during expiration the opposite procedure occurs. Associated with this jerky seesawing is a shift of the mediastinal contents to the sound side during inspiration. Among recent reports, that of Tyson alone offers any information on the prognosis. About one third of his patients made complete recovery in six months.

Purulent Parotitis in the Newborn. Dr. Irene Shmigelsky and Dr. Seyworth N. Sanford.

Five cases of purulent parotitis during the newborn period are added to the series already reported, making a total of 62 cases. However, it is believed that this condition is much more frequent than its reported incidence would indicate. A definite routine of treatment by administration of sulfathiazole and incision of the gland when fluctuation occurred resulted in the recovery of all 5 infants.

Fracture of the Clavicle in the Newborn. Dr. E. T. McEnery.

Fracture of the clavicle in the newborn is of relatively common occurrence. It is more frequent in infants born by normal spontaneous delivery than in those born by difficult extractions. Because it causes such little deformity and practically no impairment of movement, its early detection is missed in the examination of the newborn. Early recognition often saves an embarrassing explanation later, when the mother calls attention to the lump in the child's neck. This is the callus at the site of fracture.

In 1930, Sanford presented before this Society a paper on "The Moro Reflex as a Diagnostic Aid in Fracture of the Clavicle in the Newborn Period." Because of this paper I became interested in the early recognition of the condition.

The Moro, or embrace, reflex was described in 1918 as follows: "An infant is placed on a table and when the table is struck a motor reaction is obtained. The arms are suddenly thrown out in an embrace attitude, describing an arc and tending to approach one another, with a slight tremor; the fingers are at first spread and then closed." Moro found the embrace reflex to be a normal phenomenon in infants up to the age of 3 months. It is a symmetric reflex. In infants with cerebral injury it is absent. In cases of injury to the brachial plexus and of trauma to the clavicle or arm, it is unilateral in response. Because of this unilateral significance, Sanford described 6 cases of fractured clavicle, revealed in the examination of 465 newborn babies.

In the examination of several thousand newborn babies in the past thirteen years, the various stimuli to elicit the Moro reflex were used. In some infants the response was noted readily; in others it was difficult to elicit. Because of the uncertain response, a more positive method was sought for demonstration of a fractured clavicle. The method of routine examination which has given the most accurate results has been to

palpate the contours of both clavicles simultaneously, with particular attention to the presence or absence of muscle spasm, which obliterates the supraclavicular space on the affected side. The muscle spasm is set up in the insertion of the two heads of the sternocleidomastoid muscle, which obliterates the depression above the clavicle at the site of fracture. The usual site is in the middle or inner third.

In 83 cases of fractured clavicle with muscle spasm, there were 54 cases of positive unilateral Moro reflex and 29 cases of negative unilateral Moro reflex. In conclusion it may be stated that unilateral muscle spasm, together with obliteration of the supraclavicular space, is diagnostic of a fractured clavicle. This method of examination eliminates such factors as cerebral injury, brachial paralysis and fracture of the humerus affecting the Moro response.

Congenital Intestinal Obstruction in the Newborn: Report of Three Cases with Successful Results of Surgical Treatment. DR. ALFRED D. BIGGS and DR. GUY V. PONTIUS.

Atresia of the bowel signifies obliteration of the lumen. The lumen may be narrowed from external pressure; this is extrinsic obstruction.

We wish to make a few brief statements of observations made in 3 cases of intestinal obstruction; these observations coincide with those made by Ladd on a much larger series.

The diagnosis depends largely on two important symptoms. The first is vomiting, which is unlike the ordinary vomiting of the newborn. It begins early, usually the first day, and is frequent, copious, persistent and bile stained and usually nonprojectile. The second cardinal symptom is the appearance of the abdomen. It may be distended at birth, but distention usually occurs after birth. The amount of distention depends on the location of the lesion. More important is the presence of peristaltic waves.

The infant makes respiratory movements in utero; it urinates in utero; likewise, the gastrointestinal tract makes functional movements in utero. The tract is permanently a tube after the twelfth week. It probably, therefore, has six months to work against an obstruction. This accounts for the hypertrophy and enormous dilatation of the portions proximal to an atresia and also for the visible peristalsis.

Roentgenologic examination is helpful, but the barium sulfate meal is usually not necessary to establish the diagnosis. It is dangerous and causes considerable delay when time is valuable. It is an added insult to a gastrointestinal tract which is already out of adjustment.

The time element is important. The consultant seldom sees these babies before the third day. Ordinarily they must be operated on by the fourth day if the issue is to be successful.

All 3 patients were seen in consultation at outlying hospitals. All were operated on by Dr. Pontius.

REPORT OF CASES

CASE 1.—Baby P. was seen on the third day of life. He appeared normal except for dehydration from almost continuous vomiting of a thin light green fluid. He was transferred to St. Luke's Hospital the next day, improved with supporting measures and passed a slightly stained material through the anus. This led to a diagnosis of stenosis. Operation was delayed in the hope of improvement. This was a serious error; peristalsis became prominent and the baby's condition grew worse. A barium sulfate meal was given on the seventh day with inconclusive results and repeated on the eighth day. Obstruction was reported, and an operation was performed on that day.

A cyst 5 cm. in diameter lay in the right upper quadrant of the abdomen. Its wall contained all layers of the bowel. The distal portion of the jejunum angulated sharply to rise over the cyst. Struggling here, it had severed itself completely into two positions. The abdomen was filled with bowel content and barium. The postoperative condition was poor. Two and one-half grains (0.16 Gm.) of sodium sulfadiazine was ordered, to be given subcutaneously. By error, 2.5 Gm. or more than 38 grains was given. Severe nephritis followed, characterized by generalized edema with a large number of casts and blood cells. After a day or two, the wound suppurated and opened widely, almost resulting in evisceration. Gradual improvement took place; the edema disappeared after two weeks, and the urine was free from blood after four weeks. The baby left the hospital after six weeks, 3 ounces (85 Gm.) under his birth weight.

The baby is now 1 year old, and a recent series of gastrointestinal roentgenograms revealed no abnormality. He is normal except for the deformity of the abdominal wall.

CASE 2.—Baby S. was seen sixty-eight hours after birth. Three hours after birth he started to vomit a copious amount of bile-stained fluid. The great distention of the abdomen had been noted in the delivery room. Four large loops of bowel were observed in vigorous peristalsis. A diagnosis of obstruction of the bowel, probably atresia, was made. Barium sulfate was not given, and the baby was operated on seventy-one hours after birth.

At an undetermined point, the ileum ended in a blind pouch. Above this point it was enormously dilated, to approximately 35 or 40 mm. in diameter, the distended intestine practically filling the abdomen. Distally, the ileum was collapsed. It measured 7 to 9 mm. in diameter and began with a rounded end. There was no connection between the two portions. There were two large defects in the mesentery, through one of which the bowel was herniated. The portion of the bowel corresponding to these defects, measuring 118 cm. in length, or about half the small bowel, was removed. A lateral anastomosis was made.

This baby took more than the usual amount of food but gained slowly and never attained more than 6 ounces (170 Gm.) above birth weight. The stools appeared greasy and contained fat. There were frequently recurring pulmonary infections, raising the question of pancreatic disease. On the eighty-third day of life, the baby was transferred to St. Luke's Hospital. The fat disappeared from the stools. A meal of barium sulfate showed lagging at the site of anastomosis, indicating a small opening.

The baby died on the one hundred and twelfth day. Autopsy revealed that he died from inanition. The ostium was found near the middle of the ileum and was 5 mm. in diameter. The diameter of the bowel below the anastomosis had increased 100 per cent since operation, measuring 15 mm.; above, it had decreased about one third, measuring 30 mm. It was felt that the inanition resulted because about half the small bowel had been removed, although it may have been due to the insufficiently large stoma.

CASE 3.—Baby B. was seen fifty-four hours after birth. The presenting symptom was vomiting, similar to that observed in the other cases. Deep peristaltic waves were noted, progressing downward from the upper part of the abdomen into the left lower quadrant

The baby passed large amounts of meconium. The diagosis was high grade obstruction, probably atresia, cated high in the bowel; use of barium sulfate was t advised. In the roentgenogram, two large gas bbles were seen, one representing the stomach and e other the greatly dilated duodenum. No gas was en beyond the obstruction. A catheter was passed, and e gas escaped.

The baby was operated on twenty-four hours later. he duodenum was so greatly dilated that the pylorus uld not be identified. The obstruction was located in e third portion of the duodenum near the ligament Treitz. It was not dissected out. An anastomosis tween the duodenum and the jejunum was made. The stoperative course was stormy, and the baby left the spital after four weeks.

A series of gastrointestinal roentgenograms taken at e age of 4 months was shown.

ongenital Morphinism: Report of a Case. DR. M. A. PERLSTEIN.

Among the rare causes of convulsions in the newborn ust be included congenital morphinism. Although the ndition is not mentioned in any of the standard textoks on pediatrics or medicine, it seems to be fairly mmon knowledge among physicians who handle tients who are morphine addicts that children born these patients are apt to die within the first week life.

A full term girl was delivered by cesarean section a 34 year old mother who was a known morphine dict. During her pregnancy and on the day of her livery, this mother had been taking an average daily se of 10 grains (0.65 Gm.) of morphine intravenously. eventeen years previously (that is, before she became addict) she had given birth to a girl who, she stated, living and apparently normal.

The present infant weighed 7 pounds and 5 ounces ,320 Gm.) at birth and was apparently normal. There as no cyanosis or dyspnea. Symptoms first appeared the third day of life, when it was noted that the ild was irritable and restless. Although it took its od readily, it vomited and had loose bowel movements. y the end of the fourth day the symptoms became ggravated and tremors of the whole body appeared. he child by this time had lost 1½ pounds (680 Gm.) om its birth weight. It would sleep fitfully and when sturbed for feeding or for general hygiene would cry great deal, hold its breath and go into a generalized nvulsion. The administration of vitamin K and of lcium gluconate parenterally had been without demonrable benefit. Although I had never seen the condition a newborn child before, the symptoms were obviously ose due to withdrawal of morphine. Physically and eurologically the child was normal except for a palable spleen and a congenital bilateral horizontal ystagmus. The blood sugar, phosphorus and calcium vels were all normal. The lumbar puncture likewise elded a fluid which was entirely normal. A sample of lood drawn at this time revealed no traces of morphine. his, of course, could not rule out congenital morphinm, since the drug would have been entirely excreted the fifth day. It happened, however, that at this me my colleagues and I had been interested in a roblem on vernix caseosa, and all babies born during his period were having the vernix removed at birth nd saved for chemical analysis. The vernix caseosa aved for this purpose was thus available and was xamined qualitatively for morphine; evidence of the rug was found.

The treatment consisted of sedation. It was found that ⅛ grain (0.008 Gm.) of phenobarbital administered every four hours was sufficient to allay all the symptoms. Almost immediately the tremors were diminished, the vomiting and diarrhea cleared up and the child began to gain weight. From this time on, recovery was uneventful, and the child was discharged on the tenth day, weighing 1 pound (450 Gm.) less than at birth. At home the tremors were noted occasionally by the mother until the baby was 1 month old. The child was given phenobarbital according to the same dosage schedule for a period of eight weeks, after which the amount of drug was tapered off and finally stopped.

The child was followed for twelve months; it developed normally, turning over at 3 months of age and sitting alone at 7 months. The nystagmus noted at birth persisted, and when the child was 2 months old, nodding of the head and typical spasmus nutans developed, which were gradually clearing when the child was 1 year old and beginning to stand with support.

Morphine evidently passes through the placenta in sufficient amount to cause congenital addiction in the child. Withdrawal of this source of morphine after birth will naturally result in withdrawal symptoms, which if uncontrolled usually lead to convulsions and death. Although it is rare, the condition must be considered when other causes of convulsions in the neonatal period are ruled out.

MORLEY D. MCNEAL, M.D., *President, in the Chair*

Feb. 20, 1945

Caustic Strictures of the Esophagus. DR. PAUL H. HOLINGER.

The ingestion of caustics by children is still a common avoidable accident. Household lye, Clorox (sodium hypochlorite, 5.25 per cent), Drano (active ingredient, sodium hydroxide) and household ammonia (solution of ammonium hydroxide) are the most frequently swallowed alkali solutions. In almost every instance the accident occurs because the lye is placed in a cup, glass or bottle ordinarily used by the child for eating or drinking. Hydrochloric acid is the most frequently swallowed acid solution because it is kept in home workshops, usually in a pop bottle, for soldering. Lactic acid used to make lactic acid milk has produced strictures when given to infants in full strength; the error is usually due to the similarity between the bottles in which the child's cod liver oil and the lactic acid are kept. Iodine, phenol and saponated solution of cresol are the most frequent of the "medicine cabinet" accidents.

The pathologic changes produced by caustic burns of the esophagus may be divided into stages. The acute burn produces stomatitis, esophagitis, gastritis and occasionally esophageal necrosis and mediastinitis. Laryngitis and chemical bronchopneumonia may develop if some of the material is aspirated. Frequently the normal swallowing function returns after the acute symptoms subside, only to be followed by a gradually returning dysphagia. The further changes of caustic burns are concerned with development of cicatricial stenosis, which may result in complete atresia.

Immediate treatment of an acute lye burn consists of weak neutralization of the alkali by orange juice or very weak vinegar. Stronger acid solutions are caustics

in themselves and should be avoided. Sedatives are indicated because of the pain; symptoms of shock should be treated as they occur. Attempts to wash the stomach are dangerous because of possible perforation. It is generally necessary to give fluids intravenously, and often for feeding purposes a gastrostomy must be done soon after ingestion of the caustic.

Several institutions advocate immediate dilation of the esophagus, beginning the first or second day after the accident. Catheters filled with lead shot are used, and their own weight carries them to the stomach. There is danger of perforating the esophagus in the early acute stage. Active dilation may be safely started in from six weeks to two months, either by direct vision through the esophagoscope or if the child has a gastrostomy by the retrograde technic over a string. It is essential that treatment be begun during this period to avoid atresia later. If an esophageal atresia defies all efforts at canalization, reconstruction of the esophagus subcutaneously may become necessary. The tragedy in most cases of esophageal stricture is that the family, and often the physician, are not aware that normal or almost normal return of swallowing occurs after the acute edema associated with the original burn subsides. Treatment must be begun during this period of relative lack of symptoms if stricture formation is to be avoided.

Recurrent or Suppurative Parotitis. Dr. John A. Bigler.

During the past several years, my associates and I have observed more than 60 cases of recurrent swelling of the parotid glands in children from 8 months of age to 12 years. The same condition has been observed in adults. In the cases here reported the swelling occurred simply as parotitis and was not secondary to any other infection or disease; there was no relationship to the condition of the teeth, gums, tonsils or throat. The swelling may be bilateral (but is usually unilateral), or it may alternate between the parotids. Involvement of the submaxillary glands has never been observed.

There is an acute onset of the swelling, with a moderate amount of discomfort. Fever may or may not be present. Leukopenia is never present, the leukocyte count being normal or slightly elevated.

The diagnosis is made by pressing the swollen gland and milking it along Stenson's duct. A characteristic purulent material will then be seen extruding from the opening of Stenson's duct.

The swelling of the parotid lasts from a few days to several weeks. In only 1 instance has suppuration through the skin occurred. There have been from two to ten or more recurrences. On culture of the purulent material from Stenson's duct, Streptococcus viridans was found in every instance; occasionally staphylococci and pneumococci were also present. Stones, calcifications or obstructions were never found in the ducts.

There is no specific therapy. Surgical operation was never resorted to, and the sulfonamide compounds were of no value. Roentgenologic treatment seemed to cause recession of glands that had been swollen for more than a week but seemed to have little or no influence on recurrence.

Omphalocele. Dr. J. J. Mussil.

R. M., a boy, was sent to the hospital with which I am associated from another hospital on Sept. 23, 1944, at the age of 2 days, because of complete eventration of the abdominal viscera. He was born at full term by normal delivery. Examination at the time of his admission revealed an essentially normal condition except a large defect in the abdominal wall through which herniated the abdominal viscera, covered by a thin, dry, transparent membrane. The covering membrane presented two areas of necrosis about 1 cm. in diameter.

The child was taken to surgery, where it was found that the entire abdominal contents, including the liver, were outside the abdominal cavity. The defect was estimated to be from 10 to 12 cm. in diameter. The liver, passively congested, was attached by a long pedicle. The stomach and the bowel appeared to be normal. The membranous covering was excised, and the skin was undermined and closed over the viscera without any attempt to close the peritoneum or fascia. The child was returned to bed in good condition except for severe cyanosis of the legs as a result of compression of the inferior vena cava. The foot of the crib was elevated, and intravenous administration of fluids and continuous Wangensteen suction were started to keep postoperative distention at the absolute minimum; injection of sodium sulfathiazole, 3.85 grains (0.24 Gm.), every eight hours, was also started.

A week later, while the sutures were being removed, evisceration again occurred; an immediate closure was done in the operating room. Penicillin, 10,000 units every four hours, was prescribed in an attempt to avoid infection. The child was placed on a regimen for patients with pyloric abnormality. Eight days later the wound again split open, and the child was again taken to the operating room. This time three small abscesses were found, one between the liver and anterior abdominal wall, one between the stomach and abdominal wall and one in the right rectus muscle. Cultures revealed these to be caused by Staphylococcus aureus. This time it was felt that a fascial closure was necessary, so the recti muscles were brought together and the fascia closed with chromic surgical gut. Administration of penicillin was again started, as well as of fluids and whole blood by intravenous injection. The temperature remained normal, and the child made an uneventful recovery except for extreme edema of both legs and the scrotum, which subsided slowly.

This case clearly demonstrates two salient points in the handling of these patients. The first is the absolute necessity for operative closure at the earliest opportunity, and the other is the effectiveness of penicillin in preventing fatal peritonitis even in the presence of existing abscesses.

Later Note (March 28, 1945).—At 6 months of age the child was progressing satisfactorily.

Pneumococcic Meningitis. Dr. Jack M. Docter.

Pneumococcic meningitis in children is a disease associated with a high mortality rate. Prior to 1942 only 6 cases of patients under 3 years of age reported as cured were found in the literature. Since the advent of the combined use of penicillin and chemotherapy there have been many more reports of cures. The mortality rate for infants under 3 years of age is still high, however. The youngest patient reported as cured and completely recovered without neurologic sequelae to date was 6 months of age.

This report concerns a 3 month old white girl, who had been well until two weeks prior to admission to the hospital. She had had a cold during the two weeks and a draining left ear for four days. On admission she lay in opisthotonos and was stuporous. A lumbar puncture revealed pneumococci type 5. Culture of materials from the ear revealed pneumococci. Penicillin, 100,000 units daily, was given intramuscularly for twenty-two days, after which 5,000 units daily was

iven intrathecally for six days. After this there as a three day intermission followed by a recurrence f organisms in the spinal fluid. Intrathecal injection f penicillin was then resumed for five more days. The atient also received sodium sulfadiazine subcutaneously, grain (0.06 Gm.) per pound (454 Gm.) of body weight, nd later sulfapyridine and sulfathiazole orally. She as given 50,000 units of type V antipneumococcus erum intravenously.

All treatment was stopped on the thirty-ninth hosital day, and the patient was discharged on the fortyighth day. At discharge there was no evidence of eurologic sequelae, deafness or blindness.

uberculosis of Bone. Dr. Charles N. Pease.

J. W., a 2½ year old white boy, was admitted to he hospital in January 1943, with a history of a painss swelling over the medial aspect of the thigh just bove the femoral condyle. The pertinent family hisory was that the child's father had active pulmonary uberculosis. Examination revealed a well localized, luctuant swelling just above the medial condyle of the emur on its medial aspect. There was no swelling of he knee joint, and motion of the leg, both active and assive, was complete in flexion and extension. Roentenologic examination showed absorption of the medial ourth of the lower femoral epiphysis. The reaction to he Mantoux test, with a 1:10,000 dilution of old uberculin, was positive. A 2 inch (5 cm.) incision was ade over the area of swelling, and caseous material was evacuated. This appeared to be coming from beneath the reflexion of the synovia adjacent to the femoral condyle. A direct smear of the material demonstrated tubercle bacilli. Serial roentgenograms made at monthly intervals show a gradual replacement of bone in the epiphysis. Small cystic changes on the diaphysial side of the epiphysial plate, which appeared two months after the patient's admission to the hospital, are also disappearing. The knee joint is still freely movable. There is no clinical evidence that tuberculosis has attacked this joint.

It has been the experience of my associates and me that with this type of osseous involvement the knee joint becomes invaded. When this occurs, there is only one treatment, surgical fusion of the knee joint. If healing continues to progress as it has thus far, this may be one of the uncommon instances of tuberculous disease in bone adjacent to a weight-bearing joint which has healed without the necessity of fusion.

Epidermolysis Bullosa Hereditaria. Dr. E. Z. Mortimer.

Hurthle Cell Tumor of the Thyroid. Dr. William J. Morrow.

Subcutaneous Administration of Sodium Sulfadiazine. Dr. Kurt Glaser.

These papers will be published in full in later issues of the American Journal of Diseases of Children.

Directory of Pediatric Societies *

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary-General: Dr. L. Emmett Holt Jr., 477 First Ave, New York 16.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St. W., Montreal.
Place: New York. Time: Postponed indefinitely.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.

FOREIGN

Argentine Pediatric Society of Buenos Aires

President: Dr. Martin Ramón Arana, 1809 Rodriguez Peña, Buenos Aires.
General Secretary: Dr. Alfredo Larguia, Cerrito 1179, Buenos Aires.

Associação Paulista de Medicina, Secção de Pediatrias

President: Dr. Vicente Lara.
First Secretary: Dr. Armando de Arruda Sampaio.
Second Secretary: Dr. Luiz Augusto Monteiro Toledo, Av. Brigadeiro Luiz Antonio 393, 1° Andar, São Paulo, Brazil.
Time: Twelfth of every month, 8:30 p. m.

British Paediatric Association

President: Prof. L. G. Parsons, 58 Calthorpe Rd., Five Ways, Birmingham.
Secretary: Dr. Donald Paterson, 27 Devonshire Pl., London, W. 1.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen.

Nederlandische Vereeniging voor Kindergeneeskunde

President: Dr. J. H. G. Carstens, Servaasbolwerk 14ª, Utrecht.
Secretary: Dr. R. P. van de Kasteele, Laan van Poot 340, 's Gravenhage.
Place: Different places. Time: Three times a year.

Paediatrický Spolok na Slovensku

President: Dr. A. J. C. Chura, Lazaretská 11, Bratislava
Secretary: Dr. P. Rados, Lazaretská 6, Bratislava.
Place: Pediatric Clinic, University Bratislava. Time: Six times a year.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. L. F. Meyer, 29 Toelsohn St., Tel Aviv.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Prof. Norman Capon, 49A Rodney St. Liverpool, England.
Secretary: Dr. J. N. O'Reilly, 46 Harley St., London W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Sociedad Cubana de Pediatria

President: Dr. Teodosio Valledor Campo, Habana.
Secretary: Dr. Carlos Hernandez Miyares, Hospital Nuestra Señora de las Mercedes L y 21, Apartado 2430, Habana.
Place: Cátedra de Clinica Infantil, Hospital Nuestra Señora de las Mercedes y Hospital Municipal de Infancia, Habana. Time: Last Wednesday of every month.

Sociedad Ecuatoriana de Pediatria

President: Dr. Francisco de Icaza Bustamente.
Secretary: Dr. M. I. Gómez Lince, P. O. Box 69 Guayaquil.

Sociedad Mexicana de Pediatria

President: Dr. Fernando López Clares, 12/a. Medellin 191, Mexico.
Secretary: Dr. Jesus Gómez Pagola, Versalles 6 Mexico.

Sociedad de Pediatria de Córdoba

President: Dr. Juan Francisco Herrera, Córdoba Argentina.
Secretary: Dr. Bernardo Serebrinsky, Dean Funes 200 Esq. Ocaña (N.), Córdoba, Argentina.

Sociedad de Pediatría de Santiago de Cuba

President: Dr. Antonio Béguez César, Sagarra 10 Santiago de Cuba.
Secretary: Dra. Susana Texidó Vaillant, Padre Pi 57, Santiago de Cuba.
Place: Colegio Médico.

Sociedad Venezolana de Puericultura y Pediatria

President: Dr. Pedro J. Alvarez.
Secretary: Dr. Ernesto R. Figueroa, 3a Avenida 1 Bella Vista, Caracas.
Place: Hospital Municipal de Niños Jose Manuel de los Rios, Caracas.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Société de Pédiatrie de Paris

President: Dr. Leveuf, Paris, France.
Secretary: Dr. Jean Hallé, 10 bis Rue Pré aux Clercs, Paris, France.
Place: Hôpital des Enfants Maladies, 149 Rue de Sèvres. Time: 4:30 p. m., third Thursday of every month.

Uruguayan Society of Pediatrics

President: Dr. José Alberto Praderi, Eduardo Acevedo 1132, Montevideo.
Secretary: Dr. Héctor Fossatti, Durazno 1882, Montevideo.
Place: Club Medico del Uruguay, Avenida Agraciado 1464 (Piso 13), Montevideo.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Gilbert J. Levy, 188 S. Bellevue Blvd., Memphis, Tenn.
In compliance with the request of the Office of Defense Transportation and in the interest of the national war effort a meeting will not be held in 1945.

American Academy of Pediatrics

President: Dr. Joseph S. Wall, 1864 Wyoming Ave. N. W., Washington, D. C.
Secretary: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Place: Book-Cadillac Hotel, Detroit. Time: Jan. 15-18, 1945.
Region I. Place: Hotel Pennsylvania, New York. Time: April 2-4, 1946.
Region II. Place: Cincinnati, Ohio. Time: Nov. 14, 1945.

American Hospital Association, Children's Hospital Section

Chairman: Dr. Joelle C. Hiebert, 299 Main St., Lewiston, Maine.
Secretary: Dr. W. Franklin Wood, McLean Hospital, Waverly, Mass.

American Pediatric Society

President: Dr. C. Anderson Aldrich, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid Ave., St. Louis 8.

Canadian Society for the Study of Diseases of Children

President: Dr. H. S. Little, 300 Dufferin Ave., London, Ontario.
Secretary-Treasurer: Dr. Elizabeth Chant Robertson, 67 College St., Toronto 2.

Society for Pediatric Research

President: Dr. Edward M. Bridge, 219 Bryant St., Buffalo, N. Y.
Secretary: Dr. Mitchell I. Rubin, 1740 Bainbridge St., Philadelphia 46.

SECTIONAL

Intermountain Pediatric Society

President: Dr. Robert Alway, University of Utah School of Medicine, Salt Lake City 2.
Secretary-Treasurer: Dr. L. Paul Rasmussen, 1020 Boston Bldg., Salt Lake City 1.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

New England Pediatric Society

President: Dr. William P. Buffum, 122 Waterman St., Providence, R. I.
Secretary-Treasurer: Dr. James Marvin Baty, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Three meetings a year, occurring from September to May.

North Pacific Pediatric Society

President: Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Ore.
Secretary: Dr. C. G. Ashley, 833 S. W. 11th Ave., Portland, Ore.

Northwestern Pediatric Society

President: Dr. George B. Logan, 102 Second Ave. S. W., Rochester, Minn.
Secretary-Treasurer: Dr. Northrop Beach, 1009 Nicollet Ave., Minneapolis.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Rocky Mountain Pediatric Society

President: Dr. G. R. Fisher, 23 E. Pikes Peak Ave., Colorado Springs, Colo.
Secretary: Dr. Joseph H. Lyday, 1850 Gilpin St., Denver.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. William Weston Jr., 1428 Lady St., Columbia, S. C.
Secretary: Dr. Angus McBryde, 604 W. Chapel Hill St., Durham, N. C.

STATE

Alabama Pediatric Society

President: Dr. Jerome C. Chapman, 2160 Highland Ave., Birmingham.
Secretary-Treasurer: Dr. Ruth Berrey, 2021-6th Ave. N., Birmingham.

Arizona Pediatric Society

President: Dr. Vivian Tappan, San Clemente, Tucson.
Secretary: Dr. Hilda Kroeger, Arizona State Health Dept. (Maternal and Child Welfare Division), Phoenix.

Arkansas State Pediatric Association

Chairman: Dr. C. B. Billinsgsley, 1425 N. 11th St., Fort Smith.
Secretary: Dr. R. E. Weddington, 1425 N. 11th St., Fort Smith.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Charles W. Leach, 2000 Van Ness Ave., San Francisco 9.
Secretary: Dr. Chester I. Mead, 1930 Truxton Ave., Bakersfield.

Florida State Pediatric Society

President: Dr. Ludo Von Meysenbug, Box 3356, Daytona Beach.
Secretary: Dr. Robert Blessing, 409 Blount Bldg., Ft. Lauderdale.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Ruskin King, 10 W. Taylor St., Savannah.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. Edward T. Wakeman, 129 Whitney Ave., New Haven.
Secretary: Dr. Herman Yannet, Southbury Training School, Southbury.
Time: Three meetings a year.

Illinois State Medical Society, Section on Pediatrics

Chairman: Dr. Craig D. Butler, 715 Lake St., Oak Park.
Secretary: Dr. A. J. Fletcher, 139 N. Vermilion, Danville.

Indiana State Pediatric Society

President: Dr. K. T. Knode, 1105 E. Jefferson Bldg., South Bend.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Mark L. Floyd, Children's Hospital, Iowa City.
Secretary-Treasurer: Dr. James Dunn, Davenport Bank Bldg., Davenport.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Carl H. Laws, 12 Pierrepont St., Brooklyn, N. Y.
Secretary: Dr. George R. Murphy, 292 Madison Ave., New York.
Place: Same as State Society. Time: Same as State Society.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. Elwood W. Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary: Dr. P. F. Lucchesi, Philadelphia Hospital, Philadelphia.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Donald J. Barnes, 3001 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. Mark F. Osterlin, Central Michigan Children's Clinic, Traverse City.
Place: Detroit. Time: September 1945.

Mississippi State Pediatric Society

President: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Secretary: Dr. Guy Verner, 126 N. Congress St., Jackson.

Nebraska Pediatric Society

President: Dr. John L. Gedgoud, University of Nebraska Hospital, Omaha.
Secretary-Treasurer: Dr. Gerald C. O'Neil, 640 City National Bank Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

New Hampshire Pediatric Society

President: Dr. MacLean J. Gill, 14 N. State St., Concord.
Secretary-Treasurer: Dr. Ursula G. Sanders, 46 Pleasant St., Concord.
Time: Twice yearly.

North Carolina Pediatric Society

President: Dr. Arthur H. London Jr., 1105 W. Main St., Durham.
Secretary: Dr. Jay M. Arena, Duke Hospital, Durham.

Northern California Pediatric Society

President: Dr. John Mott Rector.
Secretary: Dr. George Bates, 490 Post St., San Francisco.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma State Pediatric Society

President: Dr. G. R. Russell, 604 S. Cincinnati Ave., Tulsa.
Secretary: Dr. Luverne Hays, 108 W. 6th St., Tulsa.
Place: With Oklahoma State Medical Association. Time: Annual Meeting.

South Carolina Pediatric Society

President: Dr. Lonita Boggs, 301 E. Coffee St., Greenville.
Secretary-Treasurer: Dr. Hilla Sheriff, 429 Wade Hampton Office Bldg., Columbia 10.

Texas Pediatric Society

President: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Secretary-Treasurer: Dr. John E. Ashby, 3610 Fairmount Ave., Dallas.

Virginia Pediatric Society

President: Dr. L. E. Sutton Jr., Medical College Hospital, Richmond.
Secretary: Dr. Emily Gardner, 1100 W. Franklin St., Richmond 20.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. Andrew Amick, 1021 Quarrier St., Charleston.
Secretary: Dr. A. A. Shawkey, Professional Bldg., Charleston.

LOCAL

Academy of Medicine of Cleveland Pediatric Section

Chairman: Dr. Charles L. Ruggles, 10515 Carnegie Ave., Cleveland.
Secretary: Dr. Walter Heymann, 2103 Adelbert Rd., Cleveland.
Place: Cleveland Medical Library Bldg. Time: 8:15 p. m., October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. John M. Ross, 530 St. Claire Ave. W., Toronto, Canada.
Secretary: Dr. J. H. Ebbs, 13 Queen's Park, Toronto, Canada.
Place: Academy of Medicine. Time: Third Thursday of each month.

Bronx Pediatric Society

President: Dr. Jacob H. Turner, 121 W. 197th St., New York.
Secretary: Dr. Harry S. Pizer, 1726 Davidson Ave., New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Kenneth G. Jennings, 159 Midwood St., Brooklyn.
Secretary: Dr. Joseph Battaglia, 713 Bushwick Ave., Brooklyn 21.
Place: Granada Hotel. Time: 8:45 p. m., fourth Wednesday of each month except May, June, July, August and September.

Buffalo Pediatric Society

President: Dr. A. Wilmot Jacobsen, 187 Bryant St., Buffalo, N. Y.
Secretary: Dr. Richard A. Downey, 786 Forest Ave., Buffalo 9, N. Y.
Place: Children's Hospital, 219 Bryant St. Time: 8:30 p. m., first Monday of each month from September to June.

Central New York Pediatric Club

President: Dr. Arthur W. Benson, 2 St. Pauls St., Troy.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Places: Various cities in New York. Time: Third Tuesday of April and October.

Chicago Pediatric Society

President: Dr. Louis W. Sauer, 636 Church St., Evanston, Ill.
Secretary: Dr. Henry G. Poncher, 1819 W. Polk St., Chicago 12.
Place: Children's Memorial Hospital, 707 Fullerton Ave. Time: Third Tuesday of each month.

Cincinnati Pediatric Society

President: Dr. Theodore K. Selkirk, 3605 Edwards Rd., Cincinnati.
Secretary: Dr. John H. Hunt, Kemper Lane Bldg., Cincinnati.
Place: Children's Hospital, Elland Ave., Cincinnati. Time: On call.

Dallas Pediatric Society

President: Dr. Robert A. Knox, 3701 Fairmount Ave., Dallas 4, Texas.
Secretary-Treasurer: Dr. Gladys J. Fashena, 4585 Belfort Pl., Dallas 4, Texas.
Place: Children's Medical Center: Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. Philip J. Howard, 2977 W. Grand Blvd., Detroit, Mich.
Secretary: Dr. John C. Montgomery, 564 Fisher Bldg., Detroit 2, Mich.
Place: Wayne County Medical Society. Time: 8:30 p. m., second Wednesday of each month, four meetings a year.

Fulton County Medical Society, Pediatrics Section (Atlanta, Ga.)

Chairman: Dr. Don F. Cathcart, 478 Peachtree St. N. E., Atlanta.
Secretary: Dr. Harry Lange, 478 Peachtree St. N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Raymond Cohen, 2300 Caroline St., Houston, Texas.
Secretary: Dr. Betty Moody, 526 Richmond Rd., Houston, Texas.
Place: College Inn, Houston. Time: Fourth Monday of each month.

Kansas City (Missouri) Pediatric Society

President: Dr. Edwin H. Schorer, 1103 Grand Ave., Kansas City.
Secretary: Dr. H. E. Petersen, Kirkpatrick Bldg., St. Joseph, Mo.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. Milo B. Brooks, 1033 Gayley Ave. W., Los Angeles.
Secretary-Treasurer: Dr. Elena Boder, 1830½ Lucille Ave., Los Angeles 26.
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd. Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Abraham M. Litvak, 1145 Eastern Parkway, Brooklyn.
Secretary: Dr. Harold Levy, 750 St. Marks Ave Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: 9:00 p. m fourth Monday of each month, October to April inclusive.

Medical Society of the County of Queens, Inc. Section on Pediatrics

Chairman: Dr. Meyeron Coe, 217-02-91st Ave., Queens Village, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Medical Society of the District of Columbia, Section on Pediatrics

President: Dr. Harry A. Spigel, 2647 Connecticut Ave., Washington, D. C.
Secretary-Treasurer: Dr. Perry W. Gard, 2520 Woodley Rd., Washington, D. C.
Place: Medical Society Bldg., 1718 M St. N. W. Time: 8 p. m., fourth Thursday of every month.

Memphis Pediatric Society

President: Dr. W. L. Rucks, 1074 Madison Ave., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry J. Jacobson, 1193 Madison Ave., Memphis, Tenn.

Milwaukee Pediatric Society

President: Dr. M. G. Peterman, 411 E. Mason St., Milwaukee 2.
Secretary-Treasurer: Dr. B. J. Malnekoff, 3213 N. Marietta Ave., Milwaukee 11.
Place: Milwaukee Children's Hospital. Time: Second Wednesday in February, April, June, October and December.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Alfred E. Fischer, 73 E. 90th St., New York.
Secretary: Dr. Robert O. Du Bois, 122 E. 76th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northern California Pediatric Society

President: Dr. John Mott Rector, 2000 Van Ness Ave., San Francisco.
Secretary: Dr. George Bates, 490 Post St., San Francisco 2.
Place: San Francisco. Time: Second Thursday of February, April, September and November.

Oklahoma City Pediatric Society

President: Dr. William M. Taylor, 625½ N. W. 10th St., Oklahoma City.
Secretary: Dr. Jeanne Shotstall, 625½ N. W. 10th St., Oklahoma City.
Place: Oklahoma Club. Time: Third Thursday of each month.

Philadelphia Pediatric Society

President: Dr. Ruth Hartley Weaver, 1719 Rittenhouse St., Philadelphia.
Secretary: Dr. Sherman Little, 1740 Bainbridge St., Philadelphia 46.
Place: College of Physicians, 19 S. 22d St. Time: 8:30 p. m., second Tuesday in October, December, February and May.

Pittsburgh Pediatric Society

President: Dr. Elwood Stitzel, 403 Central Trust Bldg., Altoona, Pa.
Secretary-Treasurer: Dr. C. J. Stoecklein, Medical Arts Bldg., Pittsburgh 13.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to June, inclusive.

Puget Sound Pediatric Society

President: Dr. D. M. Dayton, 740 St. Helens Ave., Tacoma.
Secretary: Dr. W. B. Chesley, 1306 Madison St., Seattle 4.
Place: College Club. Time: Third Friday of each month from September to June at 6:30 p. m.

Richmond Pediatric Society

President: Dr. T. Stanley Meade, 913 Floyd Ave., Richmond, Va.
Secretary-Treasurer: Dr. Edwin L. Kendig Jr., 828 W. Franklin St., Richmond 20, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: 8 p. m., third Thursday of each month except June, July and August.

Rochester Pediatric Society

President: Dr. William L. Bradford, 260 Crittenden Blvd., Rochester 7, N. Y.
Secretary-Treasurer: Dr. Donald D. Posson, 222 Chili Ave., Rochester 11, N. Y.
Place: Rochester Academy of Medicine or arrangement by program committee. Time: Third Friday of each month from October to May.

St. Louis Pediatric Society

President: Dr. Joseph C. Jaudon, 337 N. Euclid Ave., St. Louis.
Secretary-Treasurer: Dr. Gilbert B. Forbes, 500 S. Kingshighway, St. Louis.
Place: Branscome Hotel. Time: 7:00 p. m., third Thursday of each month from November to June.

Southwestern Pediatric Society

President: Dr. William Belford, 420 Walnut St., San Diego, Calif.
Secretary: Dr. Robert J. Dostal, 710 Wilshire Blvd., Santa Monica, Calif.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Park Bradshaw, Muskegon, Mich.
Secretary: Dr. Harry A. Towsley, University of Michigan, Department of Pediatrics and Communicable Diseases, Ann Arbor, Mich.

Westchester County Medical Society, Pediatrics Section (New York)

President: Dr. John B. Ahouse, 27 Ludlow St., Yonkers, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 64 Highland Rd., Rye, N. Y.
Place: Hospitals of Westchester County. Time: Third Thursday in November, January, March and May.